



ROYAL COMMISSION OF INQUIRY INTO CERTAIN DEATHS AT THE HOSPITAL FOR SICK CHILDREN AND RELATED MATTERS.

> Hearing held 8th floor 180 Dundas Street West Toronto, Ontario

The Honourable Mr. Justice S.G.M. Grange

P.S.A. Lamek, Q.C.

E.A. Cronk

Thomas Millar

Commissioner

Counsel

Associate Counsel

Administrator

Transcript of evidence for

October 20, 1983

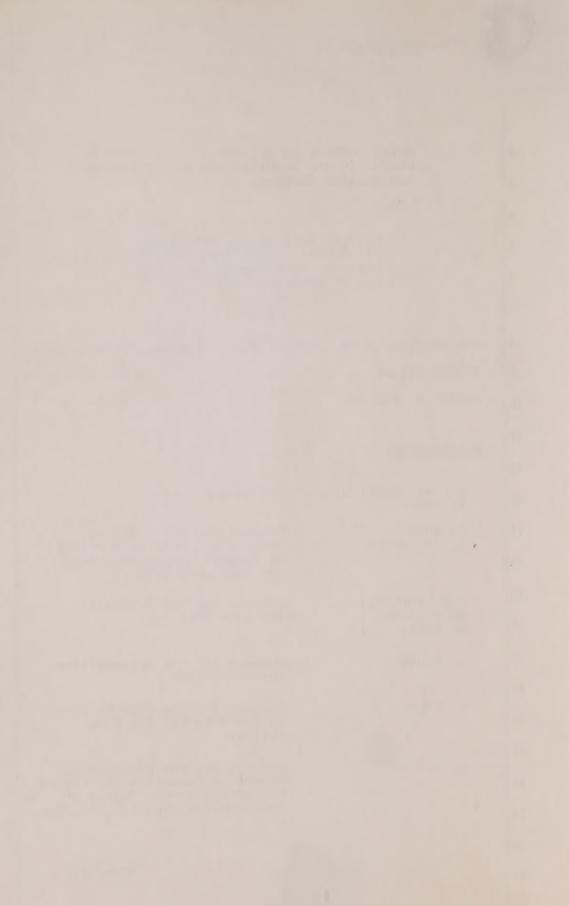
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1 ROYAL COMMISSION OF INQUITRY INTO CERTAIN DEATHS AT THE HOSPITAL FOR SICK CHILDREN AND RELATED MATTERS. 3 4 Hearing held on the 8th Floor, 5 180 Dundas Street West, Toronto, Ontario, on Thursday, the 20th 6 day of October, 1983. 8 THE HONOURABLE MR. JUSTICE S.G.M. GRANGE - Commissioner THOMAS MILLAR 0 - Administrator - MURRAY R. ELLIOT - Registrar 10 11 APPEARANCES: 12 P.S.A. LAMEK, Q.C.) Commission Counsel 13 E. CRONK Counsel for the Attorney D. HUNT 14 General and Solicitor General L. CECCHETTO) of Ontario (Crown Attorneys 15 and Coroner's Office) 16 Counsel for The Hospital I.J. ROLAND) M. THOMSON for Sick Children 17 R. BATTY 18 Counsel for The Metropolitan D. YOUNG Toronto Police 19 Counsel for numerous Doctors K. CHOWN at The Hospital for Sick 20 Children 21 Counsel for the Registered Nurses' Association of Ontario F. KITELY 22 and 35 Registered Nurses at The Hospital for Sick Children 23 24 (Cont'd)





1	APPEARANCES (Conti	nued):
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8	S. LABOW	Counsel for Mr. & Mrs. Gosselin, Mr. & Mrs. Gionas, Mr. & Mrs.
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12		deceased child Amber Dawson)
13	W.W. TOBIAS	Counsel for Mr. & Mrs. Hines (parents of deceased child Jordan Hines)
14	T GUTNELIOPE	Counsel for Lorie Pacsai and
15	J. SHINEHOFT	Kevin Garnett (parents of deceased child Kevin Pacsai).
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21		VOLUME 53
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INDEX of WITNESSES

Name	Page No.
CIMBURA, George (Resumed)	1752
Cross-Examination by Mr. Roland Cross-Examination by Ms. Kitely Cross-Examination by Mr. Olah Further Cross-Examination by Ms. Kitely Cross-Examination by Ms. Jackman Cross-Examination by Mr. Labow Cross-Examination by Mr. Tobias Cross-Examination by Mr. Shanahan Cross-Examination by Mr. Shinehoft Re-Direct Examination by Mr. Lamek	1752 1810 1840 1886 1892 1909 1912 1928 1956



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--- Upon commencing at 10:00 a.m.

THE COMMISSIONER: I guess, Mr. Roland, you are next.

MR. ROLAND: Yes.

GEORGE CIMBURA, Resumed

CROSS-EXAMINATION BY MR. ROLAND:

Q. Now, Mr. Cimbura, before we get started on questions about your methodology and your reports, I understand you have today with you, or at least are able to tell us today what reports and literature you were referring to in giving therapeutic and fatal toxic ranges for digoxin concentrations in heart muscle and lung and liver tissue. Is that so?

A. I understood it to be lung tissue and liver tissue.

Q. Yes.

A. Yes. I have looked at my notes

Q. Yes.

A. And I have some literature citations that were noted by me some time, and I have those available.

Q. All right. I take it you are not sure whether you had those citations at the time you did these ranges - set these ranges out - or at some later stage?

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A. Well, with some of them it is

Yes. Q.

A. With some I believe I did use them at the time.

> Q. All right. Now are there a lot

A. I can list them if you wish me to.

Would you mind? Q.

With respect to lung tissue it A. was a report prepared by Aderjan, A-d-e-r-j-a-n, and other authors, and was published in Archives of Toxicology 42, pages 107 to 114, 1979. This I believe referred to the levels on therapy.

Q. Yes. What ranges did that article provide for therapy?

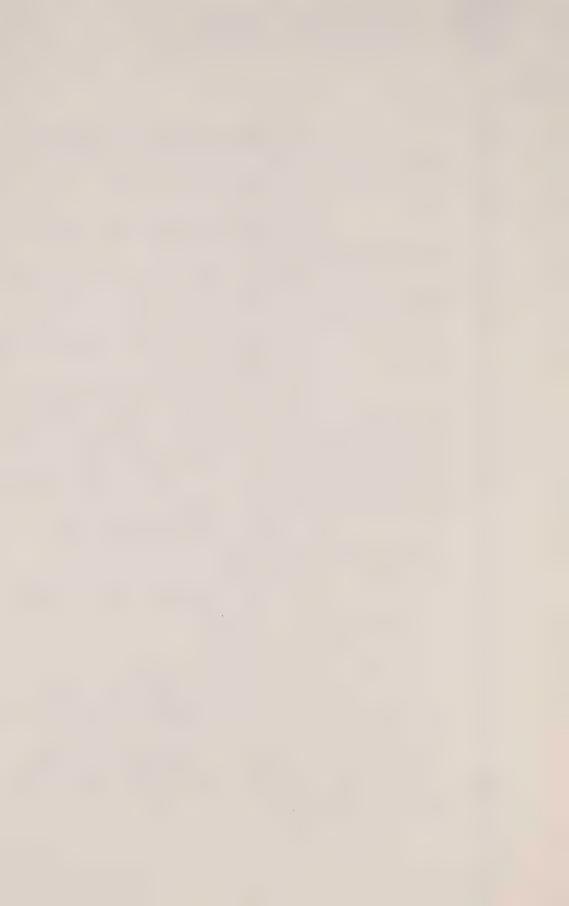
> Well, I haven't read the ranges. A.

All right. Q.

A. Recently.

All right. Sorry. Q.

I have a notation and I don't know if it is based from some notes I prepared previously in this paper - a value of 16.2 plus or minus 8.1, but I haven't - last night I haven't read all these papers again.



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I appreciate that. All right. Well, look them up ourselves and perhaps you could can give us the other citations.

A. Yes. Regarding concentrations found in poisoning cases with respect to lung tissue a paper authored by Sedgwick, S-e-d-g-w-i-c-k, and other authors, Clinical Toxicology, 18(8), 887 to 893. Year 1981. Second, also a paper I just previously mentioned, the Aderjan Paper.

> Q. Yes.

As well has some data on poisoning cases.

Another paper by Selesky, spelled S-e-l-e-s-k-y, and other authors, published in Journal of Forensic Sciences, 22(2), page 409 to 417; the year 1977.

Also a paper by Steentoft, spelled S-t-e-e-n-t-o-f-t, published in ACTA Pharmacological and Toxicological, Volume 32, pages 353 to 357, 1973. This is with respect to lung tissue, and as I said, I am not really certain whether that was the exhaustive list at the time that I had.

Liver tissue with respect to concentrations on therapy, Anderson and other authors, ACTA PED. - I assume that is Paediatric - Scandinavian,



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Volume 64, page 497, 1975. Another paper by

Karjaleinen, spelled K-a-r-j-a-l-e-i-n-e-n, and other

authors, ACTA Pharmacological and Toxicological,

Volume 34, page 385; year, 1974.

Aderjan also, which I have cited previously, I believe has some information to that effect, and Sedgwick which I have mentioned previously also some information I believe in that respect.

And with respect to concentrations found in poisoning, Selesky and others which I have mentioned already, Sedgwick and others, which I have mentioned already, Dixon and Blazey, Forensic Science, Volume 9, 145, 1977; Aderjan et al which I have already cited, and Steentoft which I have already cited.

Q. Thank you. Now turning to Exhibit 213 at page 5 of that exhibit you have given us your interassay precision studies, and can you tell us in the course of doing your various RIA runs did you run more than one control per run? What was your standard practice in terms of controls?

A. Could you help me find the document, please?

Q. Sorry, yes. It is the one that was put in evidence yesterday, and I think it is Exhibit 213.



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1 2 MR. LAMEK: It is your collection of papers. 3 MR. ROLAND: And on page 5. You have 4 given us your mean and your standard deviations. 5 MR. HUNT: Just give us one second 6 here, Mr. Roland. 7 THE COMMISSIONER: Page 5? 8 MR. ROLAND: Page 5, yes. 9 THE WITNESS: And what was your question regarding? 10 MR. ROLAND: Q. Those are your results. 11 In the course of doing your various RIA runs on samples 12 did you have more than one control or did you have 13 more than one control or how many did you have? 14 A. You mean any samples that we 15 analyzed or just --16 Yes. When you did an RIA run, the samples that you analyzed? 17 And for any samples or just for 18 this experiment? 19 No, for any sample. 20 For any sample? A. 21 Yes. 0.

Q.

We used a minimum of one control.

Yes. How many did you generally

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use?

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A.6	
2	A. We may have used a second one.
3	Q. Yes.
4	A. Sometimes, but I am not sure.
5	would have to check more details. But a minimum of
6	one.
7	Q. And when you did this precision
	study can you tell us with respect of each particular
8	run how many tubes did you have? You have said that
9	there are 86 different assays performed?
10	A. Yes.
11	Q. How many tubes did you have
12	with respect to each run?
13	A. With respect to each assay?
14	Q. Yes.
	A. I couldn't - I would have to go
15	back to the assays.
16	Q. In this study?
17	A. Yes.
18	Q. I take it you had more than one?
19	A. Tubes for what?

Q. For running these 86 different assays performed in the period.

Well, each assay would have a varying amount of tubes.

> Yes. Okay. Q.

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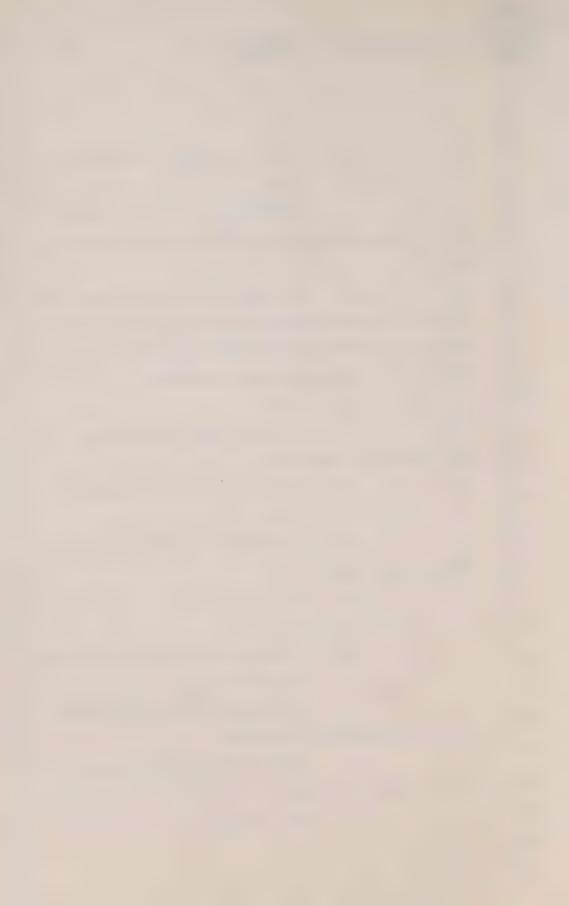
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exactly.

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A. You know, sometimes our assays may have had up to 74 tubes altogether.

Q. Right.

A. Sometimes they had less tubes, depending on how many samples we put with each assay.

Q. All right. So that I understand, this 86 different assays is the very assays that you performed in the course of carrying out the work of your report which is put in as Exhibit 95. Is that correct? Is that how I understand it?

A. Yes. These are 89 assays --

Q. 86 I think it is.

A. Sorry, 86 assays.

Q. Yes.

A. Which were used for the - at least most of which I think were used for the analyses of case samples as well.

Q. I see. All right. So then what you are telling us is each time you did these 86 assays you had at least one control tube?

A. That is right.

Q. And sometimes more than one?

A. Sometimes we may have. I would

have to check it. We did over 250 assays.

Q. Yes.

A. And I would have to check them



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Ω . I take it it is standard
practice, it is standard practice at least for
hospitals when they are doing these RIA studies
that they run two or generally three control tubes
in order to assure that there is no marked variation
in the results attained compared to the standard
serum; are you aware of that?

Α. They may run two or three.

We have had in evidence at least that the Hospital for Sick Children runs two or generally three controls when it does an RIA run. I take it you would want to do that if you were concerned about precision in order, to assure that you didn't have any substantial variation from the standard serum that you were using, or the standard in your case saline that you were using.

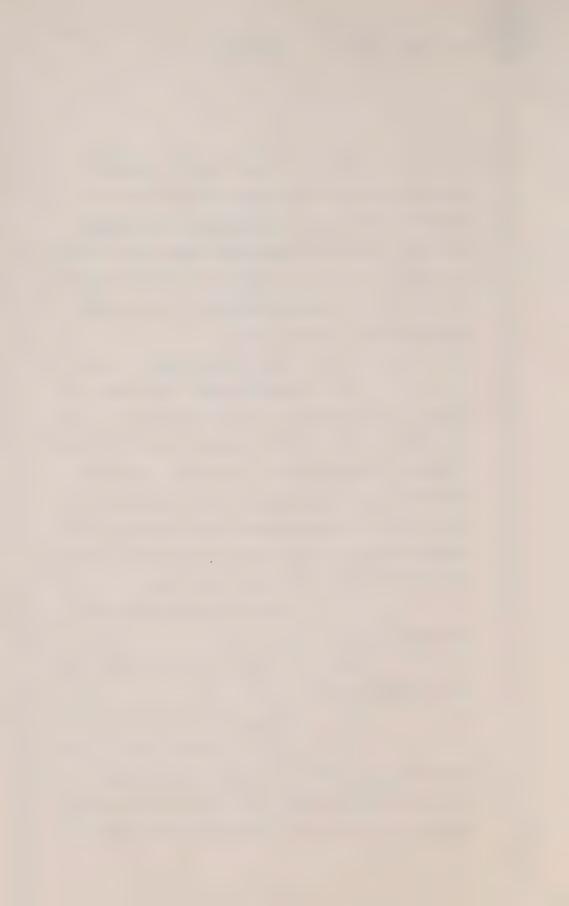
Are you saying they would want to do it?

I take it as a scientist you 0. would want to do it.

Pardon me?

Q. As a scientist I take it you.

would want to do that, you would want to use if possible more than one control per run in order to assure that you are not getting a substantial



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variation from the standard.

A. Well the value of the control that I attach to the RIA is sort of a check on any major problem with RIA.

Ω. Yes.

A. And I think one control really gives me that information.

O. Now you have told us about analyzing the samples with RIA, and then HPLC, and then you would perhaps do that several times and then reanalyze the sample by RIA. As I understand your evidence you used the HPLC from time to time in order to separate out the digoxin from the digoxin-like substances, is that right, is that how I understand it?

A. I am not sure if I understood you correctly; but for our normal procedure we don't run the HPLC several times, is that what you are saying?

 Ω .) Well, I thought you said to get some better or purer samples you had done the HPLC several times.

A. This was with respect to doing mass chromatography, mass spectrometry studies where you need a greater purity.



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	<u>Q</u> •	In any even	nt you did the
RIA	then you did the	HPLC on some	e samples and then
you	redid, analyzed t	the sample wi	th an RIA.

A. Quite often we did RIA, then we did another RIA before HPLC, and another RIA after HPLC.

 Ω . And in doing the HPLC as I understand it you were able to separate out the dig. from the dig. like substances?

A. We were able to separate out the substances that we tested.

Ω. Yes.

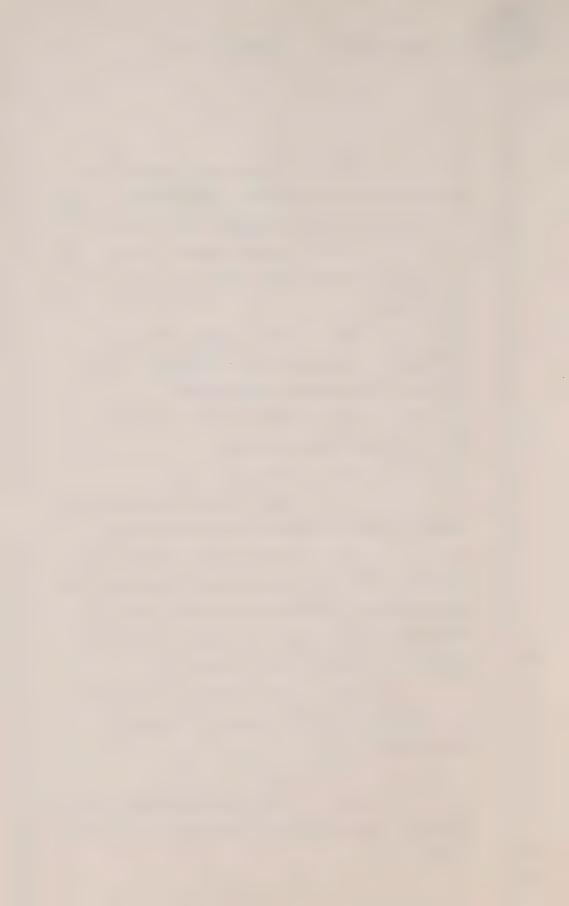
A. And I have indicated that on another document somewhere, those substances.

Ω. And you put in as,I think it is, Exhibit 215 a table showing the retention time in minutes for various substances that are run through the HPLC, and digoxin shows a retention time of 9 minutes, do you see that?

A. Yes, that is the document that I had it as "HPLC behaviour of digoxin, metabolites" is it?

O. Yes.

A. That's right, digoxin has a retention time under these conditions of 9, that is right.



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		Ω.		Aı	nd I	take	it	what	you	did
S	you ext	racted	off	in	the	HPLC	pro	cedu	re tl	ne
ul	ostances	that	had	a re	etent	tion	time	of	9 mi	nute
r	thereab	outs.								

Α. We collected a fraction, that's right.

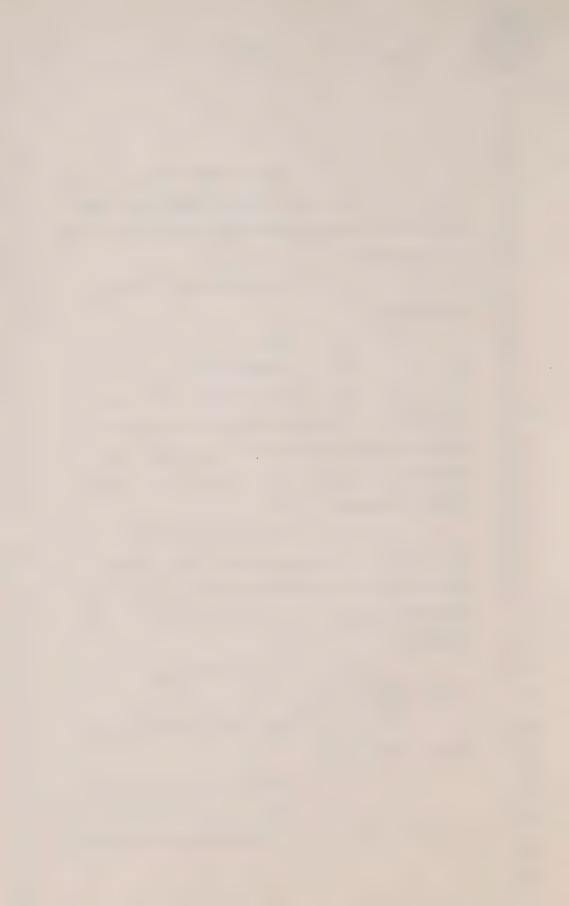
- 0. Yes.
- Α. At that time.
- And what was the range you 0. used around 9 minutes to collect the fraction, I take it wasn't precisely that one second that represents 9 minutes, but you had a time range around 9 minutes?

A. That is correct, sir. For the analysis of case materials - well usually very often it varied between 2 millilitres which would be 2 minutes, or 1.33 millilitres, or 1.33 minutes.

Q. That is the range 2 to 3 minutes around 9 minutes?

A. Where the 9 would be in the middle, that's right.

- O. 9 would be in the middle?
- Yes. Α.
- Q. So you might have as short a



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time as 7½ and as great as 10½, that will be the outside I take it?

A. Well, as I mentioned in some instances we used the 1.33 minutes.

> Yes. 0.

So if you, half of that would

O. I see, I thought I heard you say 2 minutes to 3 minutes.

> Α. No, 1.33 or 2.

O. Oh, I am sorry, so the range, the outside range would be 8 to 10?

Α. That's right. Sometimes we also use 1 millilitre but not very often.

O. Were you able to identify in the HPLC procedures what the digoxin-like substances were?

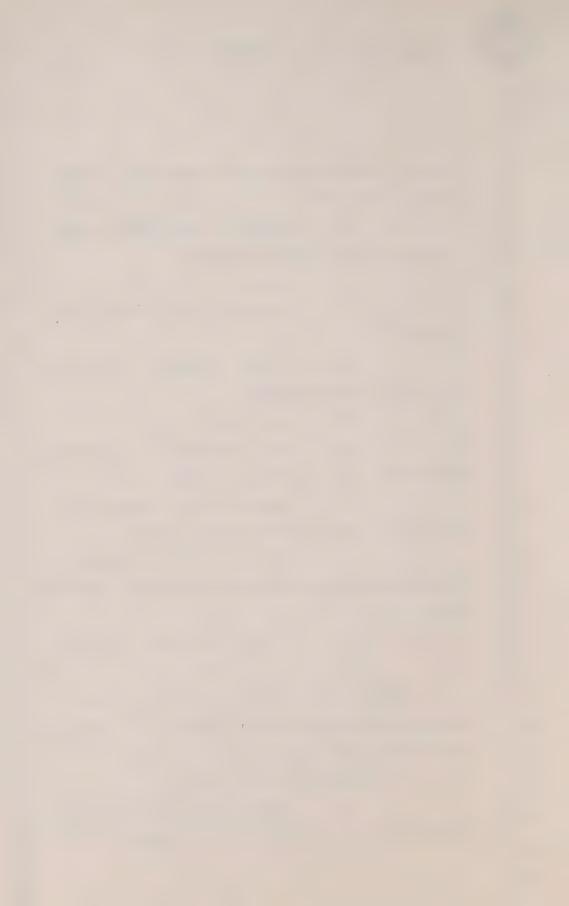
A. I don't know what you mean,

sir?

be what?

Q. Well, I take it that the digoxin-like substances, some digoxin-like substances were shown on the HPLC as well. Were you able to identify them using the HPLC process?

A. Do you mean the digoxin-like substances that I referred to in my report?



Q. Yes.

A. In the Klotz medium, is that what you are referring to?

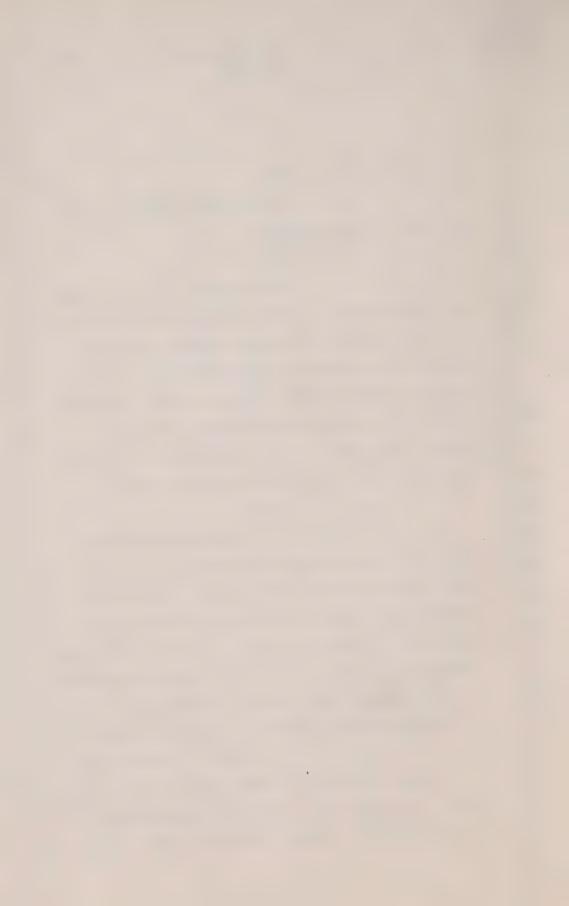
Q. Yes.

A. No, we spent some time trying to identify them. We did some research, not really very much because of our time schedule, but as I recall it we did subject the Klotz solution to - well we subjected Klotz solution to HPLC separation and we did not see an indication of other than digoxin. We didn't see any indication of any other substance under the conditions that we used it.

O. I see.

A. Which would imply to me that whatever the substances are do not elute in this time frame that we use for digoxin. We also did another study, tried to identify it by using the mass spec. in one instance as I mentioned yesterday, and again this was positive for digoxin and negative for digoxigenin, which was one of the substances we thought might be present in the Klotz medium.

Q. We will get to the mass spec, in a moment. I gather at this stage you have heard of Dr. Seccombe's work and you are familiar with other work done by others including Gruber et al



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in a review published in 1980 concerning the water loading studies of animals, and I think there are other studies like that that I presume you are familiar with that there is in the scientific community now some serious suggestions that there is a substance, and I think it has been referred to most often as substance X, that on HPLC may come off or have a retention time that is within the range that you have indicated for digoxin. Are you familiar with that?

A. Well, to answer, I have seen no studies where substance X was proven to have a similar retention time on HPLC for digoxin.

Q. But if a substance yet unidentified does have a smiliar retention time to digoxin, the kind of retention time and in the range that you have indicated, I take it then all of your findings presented in your report may have at least the possibility, let us set aside the mass spec. cases for a moment, but apart from them the possibility that there is substance X in addition to digoxin, or substance X instead of digoxin that you were analyzing by RIA and HPLC, that possibility exists I take it?

A. Well, the way you worded the



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question I think it would be a speculative possibility.

Q. Yes.

A. First of all the levels of substance X that were found were relatively very small, so that your second part of the question it could be either/or it would not be relevant and it would be speculative.





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Q. What you say is that from what you know now is with the quantities that you have been able to detect you doubt very much that substance X could represent those kinds of quantities?

On the basis of what I have Α. seen.

> Yes. 0.

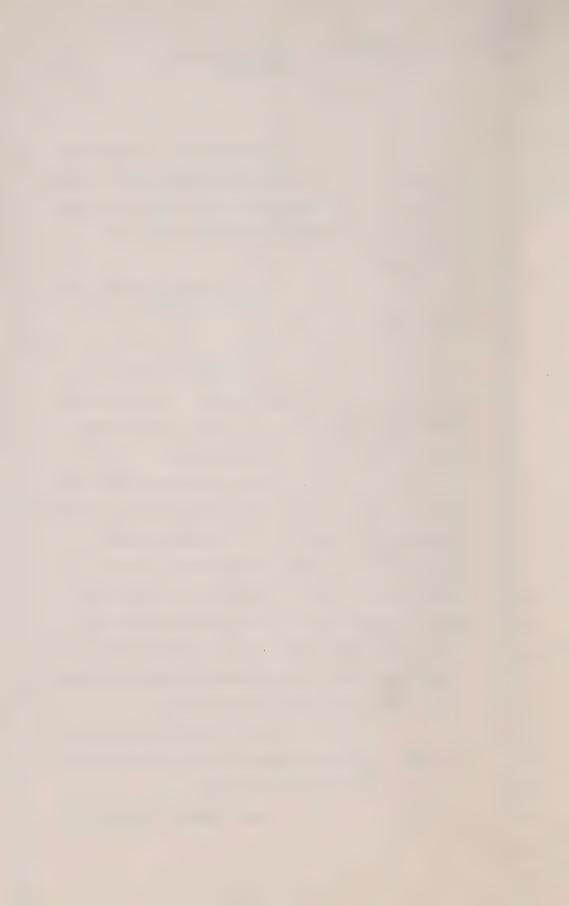
The largest values I have Α. seen were I believe around four. I cannot recall now whether one was six or not. That is the largest values I have seen in the literature.

Well, let us set aside the 0. volumes for the moment or the quantities and simply talk about the existence or non-existence of substance X as being a possibility in your procedures. I take it though that if you agree that if substance X has the same retention time range that digoxin has in your HPLC studies, that there could very well be present there a substance other than digoxin but like digoxin?

Well, if substance X has an identical retention time of digoxin then of course it would elute at the same time.

> Yes. And if it has a 0.

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retention time that is within the range you have told us of 8 to 10 or something less than that when you use 1.33 with 9 as the mean, if it was within those ranges it would elute as well?

A. That's right, if it has that range. There is one more consideration, however.

There have been no studies that I have seen that substance X was measured after extraction. All the studies that I'm aware of I recall have been done without extraction, at least as far as I am aware.

Q. Right.

A. And there is another consideration,
I should say, that in at least one child we have not
only tried one HPLC column but we have tried in
effect three different HPCL columns.

O. Yes.

A. This was the child Belanger that I believe I referred to yesterday.

Q. Yes.

A. And two of these columns were different in the reverse phase of the HPLC analysis and one column was different in the normal phase of the HPLC analysis. In addition to that, we tried another antibody, again obtaining positive results.

Q. Yes.





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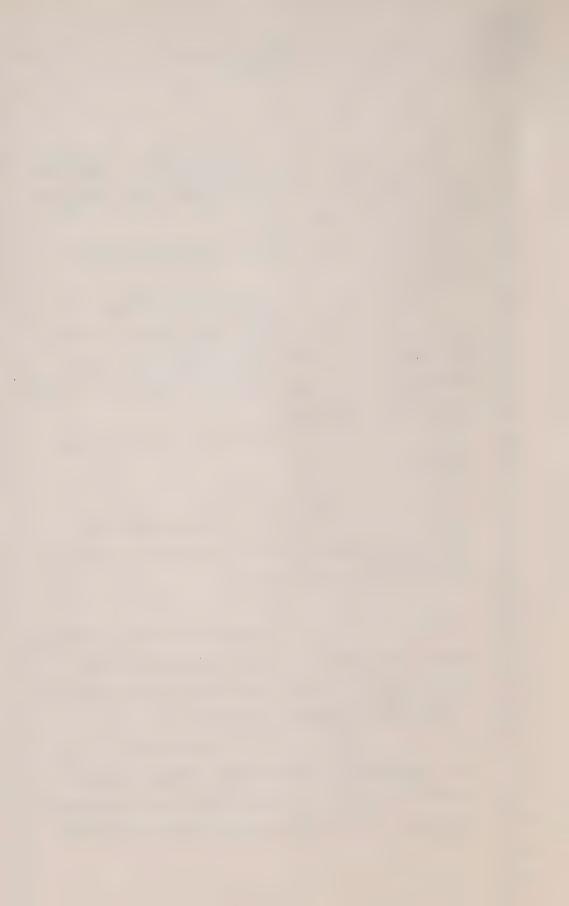
	A.	In view of that, I would have
to conclude th	at it is	very unlikely that substance
X was present	there.	
	Q.	Well, let me just ask you
this.		
	Α.	Unless it is digoxin.
	Q.	Yes. Well, let me just ask
you about what	you have	e told us about, your HPLC
procedure on B	elanger.	You told us that you did som
reverse column	s as well	1?
	Α.	Well, reverse was our usual
procedure.		
	Q.	I see.
	A. · ·	On Belanger we tried the

regular procedure in reverse as well as a different column in the reverse phase.

Q. Yes.

A. A column called micro bondapak column. In addition to that, we tried the HPLC separation in a normal phase using still a different column called porasil, as I recall it.

Q. Well, is the effect of that, those procedures on the Belanger samples that you narrow the range of retention time even further than the range that you have told us would be normal for



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an HPLC procedure?

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A. I am sorry, sir, I don't understand what you are saying.

Well, I am not sure I understand the purport of what you are telling us by doing reverse columns and so on. I presume it gives you a more precise extraction than a normal HPLC run?

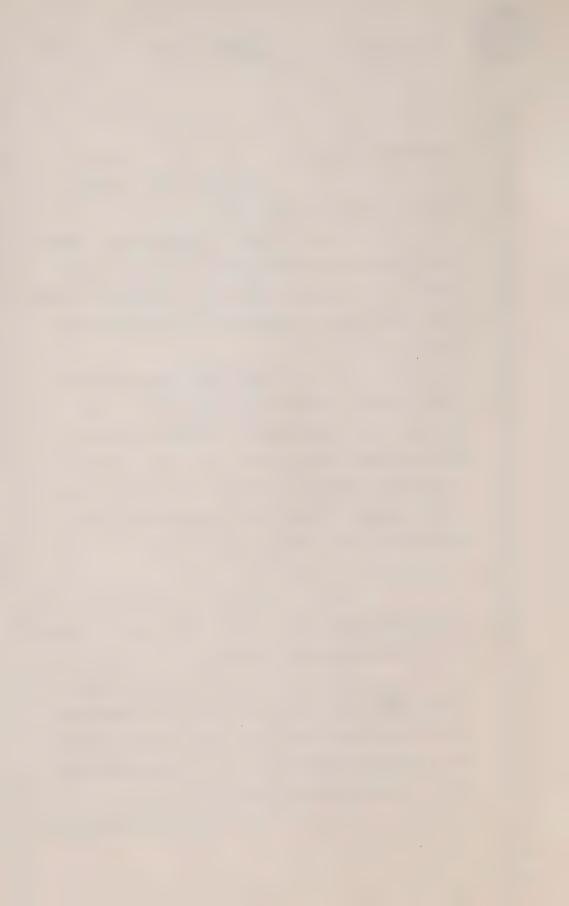
Not really from that point of view. To do a different column means that the elution, retention time will change for digoxin. So, from that point of view if it still comes from a different time it increases your certainty that it is digoxin. If you use a third column, again, the elution time, the time will change.

> 0. Yes.

And again if the digoxin comes at that different time well it still farther increases my confidence that it is digoxin.

Yes. What you are saying is Q. by doing it three different times in different ways each digoxin like substance is going to have to be very much like digoxin to be indistinguishable with those three procedures used?

That's right, and based on my



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experience and knowledge with these analyses I am satisfied to a reasonable degree what I consider of scientific evidence that it is digoxin.

Q. And dealing with mass spectrometry, you have told us that that was done with respect to a couple of samples. I gather from what I understand from mass spectrometry that it is a process whereby molecules are smashed, basically, and that what you have is particles that are split off from the molecules and that they show two things. They show a distinctive characteristic and they show a distinctive activity that helps you identify what the molecule was. Am I on line, is that basically what mass spectrometry does?

A. Well, basically, yes. I am not a mass spectroscopist myself but basically this is what happens that a molecule is bombarded by a stream of elctrons.

Q. Yes.

A. And broken into fragments and the fragments or the molecule, depending what form, there are many forms - well, not many - but different forms of analyses you can do on mass spectrometry.

Q. Yes.



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A.	But in general these	fragments
then are analysed	by instrument and can be	
characteristic of	the drug.	

Q. Yes. Of the molecule itself. You are trying to determine what that molecule is, I take it, that the particles come from and that molecule hopefully tells you what the substance is?

A. Well, again, depending on what version of mass spectrometry you do.

O. Yes.

A. From some you get more precise information with respect to molecular weight, from some you get less information. But in a sense you are always comparing a standard again with the unknown and it is under similar conditions and in a sense you are comparing the fragments that you obtain with a standard, with the fragments that you obtain from the unknown. That is in a sense what happens.

Q. And I gather what you have is a mass spectrum tracing or print-out on a piece of paper that someone who is qualified, a mass spectroscopist is capable of analyzing?

A. Well, the mass spectrometry is usually coupled with the data system which produces





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2	charts at the end, that's right.
3	Q. Yes. And do you have those
4	charts, those mass spectrum tracings from the studies
5	that you did with respect to Lombardo and the other
	one was Belanger I think?
6	A. Yes, I have some, yes.
7	Q. Yes.
8	A. I'm not sure whether they are
9	complete but I have some, yes.
0	Q. I see. Do you have the ones
1	that come from - you don't have all of them that
	came from those studies?
2	A. Well, I may have all of them.
.3	I'm not sure, I would have to get the mass spectroscopist
4	who had done it to go over them.
5	Q. Yes. Who was the person that
6	did the study?
7	A. This was Dr. Zamecnik,
8	z-a-m-e-c-n-i-k.
1	Q. I see.
.9	A. He did the final instrumentation.
20	Of course, there was a lot of work before the
21	instrumentation, as I believe I mentioned yesterday,
22	extensive purification of the sample is necessary
23	before the sample is even introduced into the equipment.



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Q. And is he the person that interpreted the tracings?

A. Yes.

Q. Yes, right. Is he with the Centre of Forensic Sciences?

A. No, he is now with another agency. He is here in Toronto.

Q. And I take it you have no experience yourself, at least not enough to interpret those tracings?

A. Well, I am familiar with them. I am not a mass spectroscopist.

Q. Yes, but I take it it takes some expertise to be able to interpret the results?

A. Well, to understand the principles.

O. Yes.

A. And to interpret it correctly under some circumstances, yes, it can take a great deal of expertise, yes.

Q. And do you have as well the criteria used to interpret those print-outs or tracings. I take it there are some criteria that have to go along with the tracings in order to understand them. Do you have that criteria as well?

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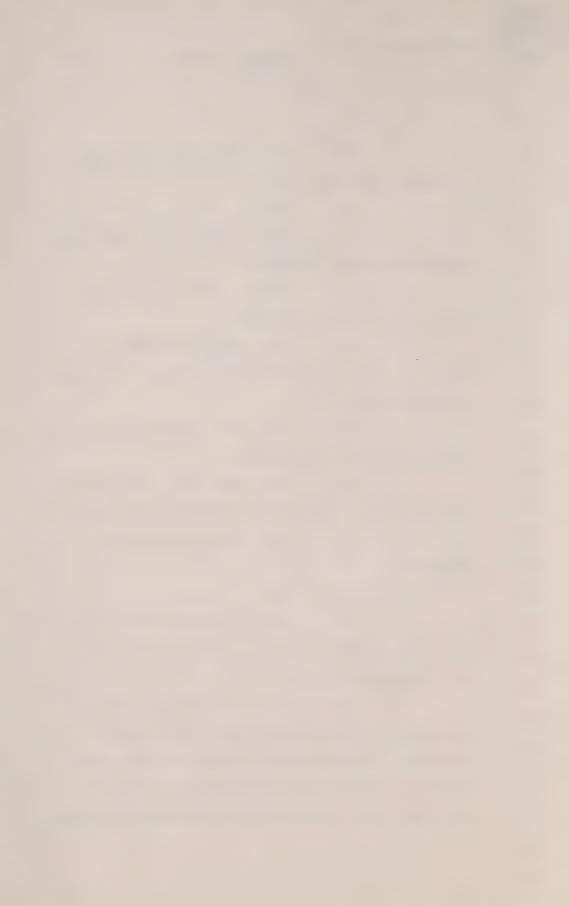
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y criteria.	Α.	I'm not	sure w	hat yo	ou mean
7	Q.	Well, I	gather	that	you ha

ve to be able to identify some known substances on the mass spectrum tracings?

A. Well, your own standard, that's what I mentioned.



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		Ω.		Yes.	And	I	gath	er y	70u	have	2
some	document	atio	n tha	t sets	out	t	hose	sta	nda	rds	as
the	criteria	you	use to	o inte	erpre	t	the	trac	eing	s?	

A. I believe so. It is a normal procedure to run standards, yes.

Q. Yes. Perhaps you could provide the tracings in that criteria setting out the standards to Mr. Lamek at some time at your convenience so that we could have a look at them or at least so that our experts could have a look at them because they seem to be very important in this case, and these matters, especially with respect to Baby Lombardo because as I understand your evidence you have indicated that you or the mass spectroscopist has positively identified digoxin in the studies that were done on the samples from Baby Lombardo.

- A. The result was positive.
- O. Yes.
- A. In his opinion.
- Q. Could you provide those documents and that material to Mr. Lamek? Is that.

possible?

THE COMMISSIONER: I think the first question is are you able to do it? Are there such?



sir.

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THE WITNESS: I believe we have them,

THE COMMISSIONER: All right. Is there any objection to their being provided?

MR. HUNT: No.

THE COMMISSIONER: Then if you wouldn't mind - all you want is you want to have your experts look at it?

MR. ROLAND: I would like to have them look at it, yes.

THE COMMISSIONER: So it is he doesn't have to rush right out now?

MR. ROLAND: No, there is no rush. It can be done at his convenience.

Q. Do you have the same documentation with respect to the work done on samples from Baby Belanger?

A. Are you referring to GC mass spec. again?

Q. Yes.

A. Yes, I believe so.

 Ω . I would like you to provide those if you could as well.

Turning to Exhibit 95 which is your report, or an accumulation of your reports, at page 4



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is it?

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Note 3 you give a range for digoxin at a therapeutic level in heart muscle --

THE COMMISSIONER: Page 4. Is this

MR. ROLAND: This is 95A, yes, and Note No. 3 at the top of page 4.

 Ω . And as well you give a range for fatal poisoning by digoxin, and it is obvious there is a very substantial overlap between those two ranges. In fact the overlap you show there is from 108 to 975.

I gather as well --

A. I am sorry, which page is it?
I am not sure exactly.

THE COMMISSIONER: This is Note 4,

MR. ROLAND: Note 3 on page 4.

THE WITNESS: Okay. That is right.

MR. HUNT: Have you got it?

MR. ROLAND: Ω . I gather in those ranges as well there was a range of toxic levels that are non-fatal; that somewhere in that range that you have given, that very broad range that you have given it can be said that there are toxic levels but non-fatal. Is that fair?



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Α.	In	wnich	range?

(Roland)

Q. Well, in the very broad range that you have given that shows an overlap, certainly between 108 as the lowest fatal poisoning range and 975 is the highest therapeutic range.

> Α. Yes.

0. I gather there is first in that range a toxic but non-fatal range as well?

Well, there may be but I have no awareness of it.

> 0. No.

Α. My range, fatal range, is compiled on the basis of death by digoxin overdose.

> Q. Yes.

My therapeutic range has been compiled on the basis of children on digoxin therapy so that I really don't - you know I cannot say whether there is, that there shouldn't be in these two ranges as I compile them.

THE COMMISSIONER: Were they all taken from children who died whether they died from the digoxin poisoning or some other --

THE WITNESS: That is correct.

THE COMMISSIONER: I suppose you are depending upon the advice of the pathologist or



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someone else as to what they died from because you have no way of knowing yourself?

THE WITNESS: Oh, yes, that is right.

The children that I have studied, the information

I had available to me is the fact that they did not die of digoxin poisoning, the ones that I have used as a control.

THE COMMISSIONER: You are not including these critical infants in your statistics because that is what this Commission is all about, to find out whether they died from digoxin poisoning or from some other causes.

So I take it you are not including any of these babies that you are investigating in your calculations?

THE WITNESS: No, sir. No, these are separate children, that is right. Separate people.

THE COMMISSIONER: Yes. Where did you get that information?

THE WITNESS: Well I --

THE COMMISSIONER: Is that part of

the tests that you have shown us here?

THE WITNESS: Yes. As far as the therapeutic range in heart of infants I have showed



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the document yesterday.

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THE COMMISSIONER: Yes.

THE WITNESS: And as far as the fatal range of course is based on literature.

THE COMMISSIONER: Yes.

THE WITNESS: But the children under investigation are not included.

MR. ROLAND: Q. And, Doctor, yesterday you showed us a therapeutic range in heart tissue I think in the neighbourhood of 300 and something, but you give as your therapeutic range an upper limit 975, and I gather that comes from the literature?

Α. That as a matter fact is the only value that I found to be so high.

> Yes. 0.

In the literature, but it is a literature value, yes. It is a value and I even recall it because it somehow doesn't fit in to all the other values. It is a work published by Gorodischer in Buffalo.

His work is "Tissue and Erythro-0. Distribution of Digoxin in Infants". cyte

> I believe that is the one. Α.

Yes. And it was published in 0.



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1975. And he shows another value in that study of some --

MR. HUNT: May we have a copy for the witness, Mr. Cimbura?

MR. ROLAND: I will show it to him.

I think Mr. Cimbura is well familiar with this study. In fact he testified from it at the Preliminary Inquiry.

MR. HUNT: That was several years ago. I don't know if he remembers it.

THE WITNESS: I recall reading this study but I haven't read it very recently.

MR. ROLAND: Well, it is a not a new study.

 Ω . It contains a value as well in another infant of 643.

A. Yes. I am just trying - some of them were autopsy and some of them were as I recall it on maintenance and some of them were taken while alive so I am trying to...this I believe is an autopsy sample.

o. All right. But the study shows other values that are higher than the ones that you found in the range of 300. It showed a value as high as 643 and 519, but I gather what you



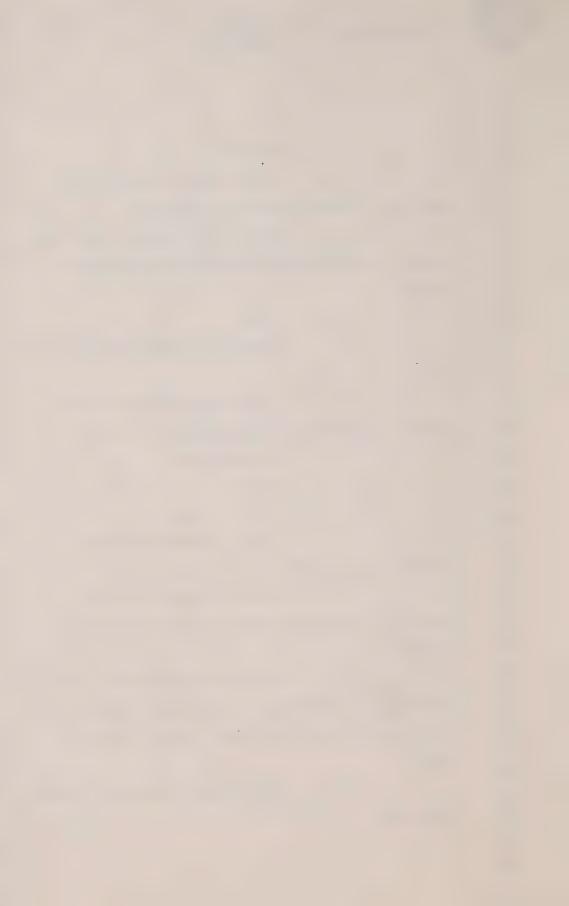
say	is	975	is	the	highest	that	you	have	seen	in	th
lite	erat	ture	?								

- A. In an infant, in a ventricle of an infant, that is right, of a heart.
 - Q. And this --
- A. In a normal as a result of normal...
- Ω . And the range between the lowest fatal measure of 108 nanograms per gram and the highest therapeutic level of 975 nanograms per gram is really quite an extraordinary broad range, isn't it?
- A. It is a wide variation, that is correct.
- Q. Yes. And I gather that is because of the various factors that affect the therapeutic as compared to the toxic results of dig. administration for various children and the various variables that exist are first age I gather. That is an important consideration? The younger the infant the higher the therapeutic range you go?
- A. In general I think that is right.
- Ω . And also the clinical condition may affect the therapeutic range?



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3	A. Such as?
	Ω . Well, such as things like
1	some renal failure and things like that.
5	A. Yes. Renal failure could have
5	caused - would result in a decreased excretion of
,	digoxin.
	Q. Yes.
	A. With accumulation at least in
	blood.
	Ω . And it may elevate what is
	a normal therapeutic range somewhat as a result.
	A. In the blood.
	Ω. Yes.
	A. That is right.
	Q. And I presume it would
	elevate it in tissue as well, wouldn't it?
	A. Well, I haven't seen any
	studies that have been done on this with respect
i	to heart.
1	Q. But there seems to be in the
	literature a broad range of therapeutic values that
1	very broadly overlap the fatal values shown for
.	digoxin.
-	A. Did you say therapeutic range
	overlaps?



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	Ω.	Yes.	The f	atal,	and it	seem	S
to be a very b	road ove	rlap so	o tha	t it i	s hard	l to	
say in any ind	ividual	in tha	t bro	ad ove	rlappi	.ng	
range of betwe	en 108 a	nd 975	from	simpl	y look	ing a	t
the values w	hether	or no	ot th	at ind	ividua	l has	
a fatal dosage	of digo	xin or	dosa	ge wit	hin th	ie	
therapeutic ra	nge.						

A. Well, I believe you are saying what I concluded that unless in fresh tissue, unless you get a value that is way either outside the normal range or else it is negative or very extremely low, you cannot - I feel I cannot make a conclusive opinion with respect to digoxin toxicity from that finding alone.

Q. I think you studied some 13 control children on digoxin therapy and I found your upper limit. It is 383. It is at page 18 of Exhibit 213. The page is titled "Digoxin Concentrations in Heart Tissue in 13 Control Children on Digoxin Therapy".

We have looked at some other studies.

There is one we have just discussed and it I think
is a study of eight children, and although there are
a number of studies they are all on fairly small
sample groups. In fact I think yours is one of the



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larger sample groups.

A. It may well be.

Q. Of the ones published. So that although we have ranges that are very broad in the end and looking at the literature in its totality we don't have results of very many children?

A. No.

O. Do we?

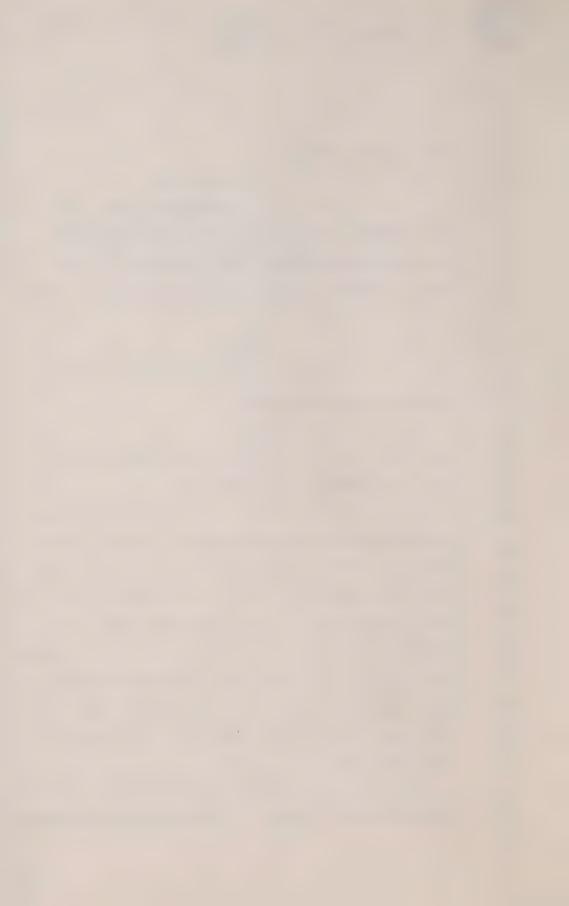
A. That is the reason why I was interested to carry out --

Q. Yes?

A. I felt it necessary to carry out this research in the beginning.

in the literature an upper range of 975 we in fact have a very small population even in total, looking at all the literature that we have looked at and that is available. I have looked at a number of studies and all the populations seem to be very small, and although 975 is the upper limit that has been shown to date we haven't seen through all the literature a very large population of children to date, have we?

A. Well, I am not really familiar exactly how many studies. I would have to go through



the literature and find out but by now I think additional studies have been published. Certainly Dr. Hastreiter's group has published one recently.

Q. Yes.

A. There may have been other studies published so - the paper that we have just discussed seems to be - appears to me to be isolated from most of the other papers with respect to the very high values found in the one paper.



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Q Turning to your therapeutic
ranges and your fatal toxic ranges for lung tissues;
as I understood your evidence the therapeutic range
that you state, first of all, between 3.4 and 30
nanograms per gram is one that doesn't come from the
literature but it comes from your own studies?

A. I believe so, I would have to look at it exactly, I forget whether that was our numbers, but I believe it was.

Q. What is the therapeutic range if you can tell us today in the various reports that you have given us the names of this morning, is it that same therapeutic range or is it higher or lower?

A. Well, in the citations that I have given this morning, are we talking about lung tissue?

O. Yes.

A. I believe it is the same because I believe that is the one that I may have used, there is only one on therapeutic and I believe that is the one I may have used when I prepared my report in January of 1982. That one I believe is within the range that I found in our research.

Since that time, the Hastreiter group has published information on lung tissue.





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Q. Your study on lung tissue is of four separate infants?

That is right, sir.

And the upper range you found was 30, and I take it that is a very small sample group for the purposes of establishing the therapeutic range for lung tissue, is it not?

Well, it is a small, relatively small number, that is right, it is useful, but the larger the number of course the more useful it would be.

Let me see if I can find it, Case No. 4, if I can find it.

THE COMMISSIONER: Page 19.

MR. ROLAND: Q. It is page 19 in

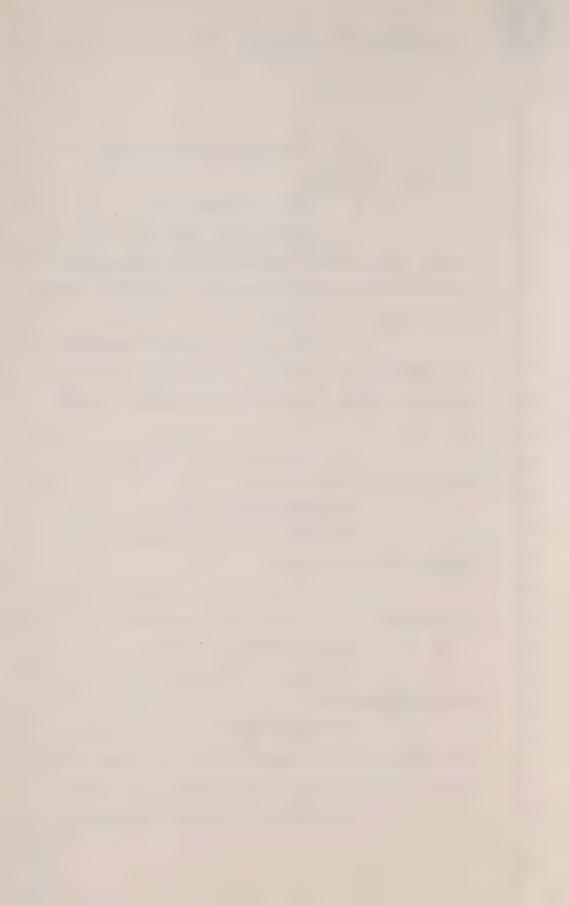
Exhibit 213 and it shows --

A. Sorry, I am not sure if I have the document, mine are not paged, I am sorry. THE COMMISSIONER: Nor was I.

MR. ROLAND: I numbered mine for

convenience purposes.

THE COMMISSIONER: I numbered mine, it just shows you how far ahead we are of everybody else. I think I stopped at 19 so if you run into trouble --MR. ROLAND: Q. Case No. 4 shows an



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interval from last dose to death of 4.5 hours. As I understand it from the evidence that we have heard so far, that is a shorter interval than is recommended for the purposes of serum digoxin testing, that you have not reached an equilibrium yet in the serum for the purposes of determining a serum level. I take it that may explain in part the 6.9 serum level that is in the next column, do you agree?

I don't know whether it would explain it.

> 0. It might explain it.

There are many other factors.

Yes. But it is one possible

explanation I take it, is it?

Well, if you consider the range in blood that I have found went up to 12.4 actually.

> Yes. 0.

So 6.9 is pretty well close to the average somewhere.

0. Well, if you hadn't reached a steady state for Infant No. 4 in the digitalizing process that was going on there, I take it that more digoxin would move from the serum to the various tissues in the body, that is the process to reach a steady state, isn't it?



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A. Well, what I understand is the equilibrium in our steady state is when the digoxin concentrations in the blood is equilibriated, or in equilibrium with the concentrations in the tissue generally, that is right.

Yes. And so one might expect if in Case No. 4 that you had not reached equilibrium or steady state that the value for the tissues including the lung tissue may go even higher, isn't that fair?

THE COMMISSIONER: I am sorry, your question was if you had not --

MR. ROLAND: If you hadn't reached steady state yet the values are going to go down in the serum and up in the tissues?

THE COMMISSIONER: What you are suggesting is the process after it reaches equilibrium in the blood.

MR. ROLAND: Yes.

Well, in the process of getting to equilibrium through the digitalizing period until you get to a steady state, basically the values go down in the serum as they rise in the tissues?

- Initially. A.
 - Yes. Then of course digoxin is



TORONTO, ONTARIO

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excreted, it is excreted I guess in a minor way during the digitalizing process, but then the values will go down both in serum and in tissue as the body excretes the digoxin, and that may be overly simplified an overly simplified description, but, however.

A. I am not clear whether I understand your question. But in any case I think, you know, the time required to reach an equilibrium under certain conditions in a tissue I haven't seen any studies for that, one could generalize, but --

Q. What I was getting at is you may have at steady state a value with respect to Infant No. 4 higher than 30, if you haven't reached steady state yet, and the digoxin is moving from the serum into the tissues, binding to the tissues including lung tissues.

THE COMMISSIONER: It is going down, isn't it? I may be wrong. I would have thought it goes down as it reaches equilibrium. It comes down, because it first goes into the blood and then of course it is a heavy concentration in the blood at the initial point.

MR. ROLAND: Yes.

THE COMMISSIONER: And eventually it reaches equilibrium which is the proper time for taking the test.





E. 6

MR. ROLAND: Exactly.

THE COMMISSIONER: So presumably assuming that there is a proper time, an equilibrium time for tissue, doesn't the same process take place there?

MR. ROLAND: Q. As I understand what happens, and maybe Mr. Cimbura cannot help us on this; the digoxin moves from the serum to bind to tissue and it binds in various quantities depending on the tissue that we are talking about, it binds more with heart tissue than it does with other tissue, some other tissue like kidneys and so on, or liver, or lung, but it binds at greater or lesser degrees depending on the tissue we are talking about, but it is basically moving from the serum during the digitalizing period to bind the tissue until an equilibrium is reached between the various tissue binding values and the serum; isn't that basically the process?

A. Generally I agree with you, yes,

basically.

Q. So during the digitalizing period up to say six or six and a half hours, you are going to have higher values in the serum relatively and lower values with tissues until you reach that equilibrium, the values with the tissue will rise





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as the values of the serum fall until the equilibrium is reached; isn't that basically the process?

I think my point, sir, was that A. I have not seen any study where the maximum amount of digoxin in a specific tissue, where the time was estimated for it.

THE COMMISSIONER: What you are suggesting is that as the level in the blood goes down the level in the tissues goes up.

MR. ROLAND: Until equilibrium is reached, that is in about six hours, I think.

THE COMMISSIONER: When is the equilibrium reached in the tissues?

MR. ROLAND: Well, the equilibrium is between the tissues and the serum and that equilibrium will be different from tissue location to tissue location because the digoxin will bind more to some tissue than to others.

THE WITNESS: That is generally what I would expect, yes.

MR. ROLAND: Q. So to follow that up; early on in the digitalizing process if an infant has not had digoxin and a therapeutic dosage is given you will find within the first half hour very high values, or relatively high values in the serum and relatively



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low	values	in	tissue	during	say	that	first	half	hour
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A. After what means of administration?

0. Well, let's say it is intravenous.

After intravenous you initially find very high levels in blood.

> 0. Yes.

And then following that there will be declining and the tissues will be rising.

Q. Yes, exactly. Turning to your report, Exhibit 95A, to begin with; I see at Note 6 on page 4 that a portion of T-41 was given to Dr. Wong for digoxin assay, Dr. Wong being a doctor at the Toronto General Hospital. Was there a result obtained from Dr. Wong?

> A. Yes, sir.

And what was that result?

That was 100 nanograms per Α.

millilitre as I recall it.

So that I take it satisfied you that your result of 91 was a more or less accurate result, at least confirmed your result?

A. Well, it was consistent with my result, that is right.

THE COMMISSIONER: Is that reported anywhere?



E.9

1 2 MR. ROLAND: I have not seen it. 3 THE COMMISSIONER: The assay of Dr. Wong's? 4 THE WITNESS: I have the report, sir. 5 THE COMMISSIONER: What did you say it 6 was, between 90 and 100? 7 THE WITNESS: 100 nanograms per milli-8 litre as I recall it. If you wish I could go through 9 my files and find the report and file it. THE COMMISSIONER: That is 100 nanograms 10 per millilitre? 11 THE WITNESS: 100 nanograms per milli-12 litre, that is right. 13 MR. ROLAND: Q. And that was a testing 14 of a whole blood sample, I gather, as the report 15 indicates? 16 Dr. Wong's result? A. 0. Yes. 17

Cimbura, cr.ex.

(Roland)

Well, I sent him a portion of the A. whole blood, I am not aware of exactly what he did with it.

Your result was done on the whole 0. blood though, wasn't it?

> That is correct, sir, yes. A.

And we know, Mr. Cimbura, do we 0.

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not, from the study that we have been looking at this morning, the study authored by Gorodischer et al, of tissue and erythrocyte distribution from digoxin in infants that with respect to infants there is, there are higher values obtained for digoxin in red blood cells or erythrocytes than with plasma, isn't that right?

A. It is a long time since I studied Gorodischer's paper. I recall something, but I believe there are more factors than that. I believe he divided children under "maintenance" and under "digitalization".

Q. Well, let's look at his paper and I am looking at page 260 and I will provide a copy of this to be put in as an exhibit.





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It shows a table of maintenance therapy and it shows a ratio between erythrocyte and plasma digoxin for children with a mean ratio of 3.62.

A. The mean with considerable variations, that's right.

Q. With considerable variations as high as 6.4 and as low as 1.06?

A. That's right.

Q. Yes. And what this study indicates, and I gather other studies like it, that you get higher values from digoxin assayed in erythrocyte than you do with digoxin assayed in plasma?

A. Well, based on this particular you make it the right range.

Q. Yes. Well, the study shows that it is never lower, it is always higher at the maintenance therapy dosage?

A. Yes.

Q. Isn't that right?

A. That's right. I recall - well,

was this maintenance that we looked at?

Q. We're looking at maintenance.

A. Maintenance, all right. I

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on	adul	ts	and	the	rat	io i	there	was	al	oout	: 1	33.	

Q. Yes, that's right. In fact, this author indicates that as well in this study that the results with respect to infants are quite different than the results that had been achieved from studies of adults and I take it that is consistent with your understanding as well?

A. Well, I would say one might expect variations, yes.

Q. Yes, all right. So, for instance, when we look at page 3 of Exhibit 95 and we see values for Sample T27 and Sample T34 and you have a value of 46 for serum and a value of 79 for red blood cells, I take it that relationship between these two values is consistent with the results obtained by Dr. Gorodischerand others in studies like the one I have just shown you.

A. Well, part of that difference could be due to that effect.

Q. Yes.

A. I am not sure of course whether it is all due to that effect.

Q. Yes, I see. When you study whole blood, I take it then you are doing a dig.



assay on both red blood cells, erythrocyte and serum and you would expect I gather a range generally higher on whole blood than you would from serum alone and lower I suppose than you would from doing erythrocyte alone?

A. Well, I am not sure if I would expect it because I have recollections of doing - this would appear that it could be based on some literature.

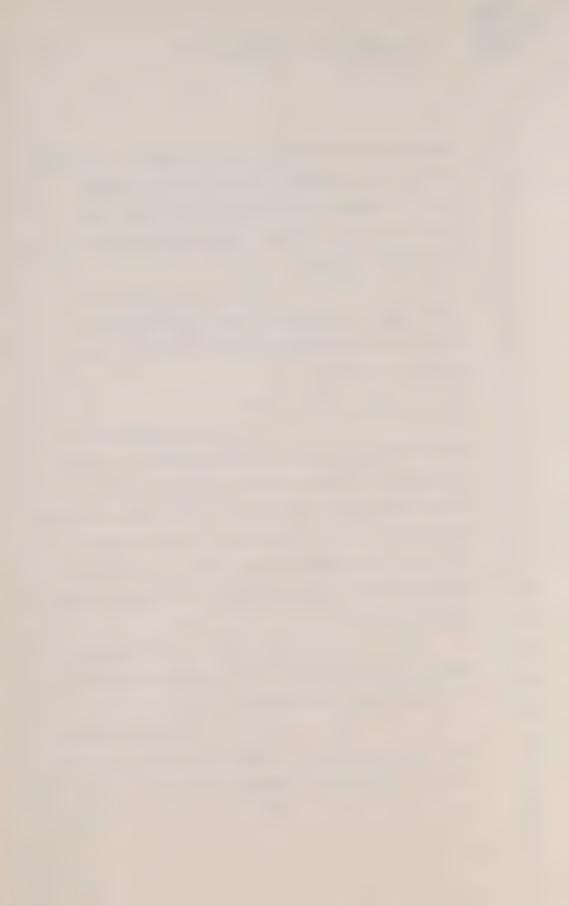
Q. Yes.

A. But I have recollections of conducting analyses in conjunction with, for example, the Hospital for Sick Children where they asked us to help them, or co-operate with them, where I believe they use serum, as I believe it, I am not certain, but this is my understanding, and I have used whole blood and yet our results were lower in some instances than in theirs.

Q. All right. Those studies I take it are not something that you have presented to us yet, that's not something that ...

A. No, I don't have a complete list of the studies. I talked to Dr. Phillips. As a matter of fact, he called me about it.

Q. Yes.



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Α.	And	apparently	he	has	a	list

Q. Well, we may see that from Dr.

Phillips.

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Dealing with Sample Tll which begins on page 1 and carries over on to page 2 of Exhibit 95, we see values for digoxin and digoxinlike substances in three tissue specimens from the heart all about the same range 36, 39 and 36 and the longest sample shows about the same range too of 32 and the fluid seems to show about the same range of 29. I gather it may be said that this generally shows an equilibrium that is being established in that entire solution of tissue and fluid?

Well, this could be a A. . . possibility of that.

> Yes. Q.

I seem to be aware that as A. I recall it now again, and it is a long time ago, but I believe that we have analysed the fluid, the Klotz medium even subsequent to this analysis and as I recall it it was even lower than that.

> 0. I see.

So, this would be against this theory, but judging by the numbers this could be a possibility.



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Q. Right. Let's deal with the
lungs for the moment. In theory I gather if you had
a solution in which you had a heart with a normal
or therapeutic range of digoxin in it and you put it
in a Klotz solution and you put a lung from, say,
another infant that hadn't been on digoxin and had
no digoxin that an equilibrium, or an attempt - I
shouldn't say an attempt, but what would happen is
that the solution would be moving towards some
equilibrium wherein the lung would take up some
digoxin, that it would move from the heart through
the fluid and that the fluid would lose some of that
digoxin to the lung which would absorb it until some
equilibrium was established?

A. Are you saying, sir, that if you place both heart and lung into the same container?

Q. Yes.

A. And the heart had digoxin in

it.

Q. Yes.

A. And the lung had no digoxin

in it initially.

Q. Yes.

A. That's right. Is that

correct?



from.

Q. Yes, the lung would take up some digoxin, wouldn't it?

A. Well, it could, I don't know.

I think under those conditions certainly I wouldn't
be sure where the digoxin in Klotz solution came

Q. I see.

A. I wouldn't be sure if I didn't know at the beginning what had what.

Q. Yes.

A. I couldn't tell where the digoxin in the Klotz solution came from, whether it came from the heart or the lung.

Q. · Yes.

A. But whether it would go back into the lung it is a possibility but I have never tried it.

Q. Well, because when I look at these values I suppose it is possible that you could have had a very much lower value in the lung initially but so long as that value was lower than the Klotz solution that it may have moved, the digoxin may have moved from the Klotz solution into the lung?

A. I would have to speculate.

I don't know, sir. There are all kinds of possibilities



and for this reason I didn't express any opinion as to the minimal, estimate of the minimal heart concentration with respect to Cook because of the fact that the two organs were contained in the same jar.

- Q. I see. Do I understand it correctly that with respect to Sample Tll, that you didn't do an HPLC on the left atrium tissue, because I see that there is no concentration of digoxin shown there?
- A. That is correct, sir. There was only RIA.
- Q. And the same can be said with respect to the Klotz solution, that you didn't do an HPLC on that?
 - A. No, that is correct, sir.
- Q. Yes. All right then if we go to Kevin Pacsai at page 4 and in particular your note about Sample T7, which is found at page 5 I am sorry, that's not the one I am looking for. Well, I'm sorry, let's turn the page, a couple of pages to Jordan Hines, page 6, that's the case I am looking for, in which you have a note about Sample T6. That sample contains tissue from the heart in three locations and Klotz fluid and it appears you



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didn't do an HPLC on the right atrium again and you didn't do an HPLC on the fluid, is that correct? That is correct, sir. 0. Yes. And yet you gave in your note, Note 1 about half way down page 7 that the concentration of digoxin in the heart before it was 6 fixed in Klotz solution was not less than 252. How can you say that, Mr. Cimbura, when you don't 8 know how much of the Klotz solution is digoxin and how much is digoxinlike substances? Well, I believe, sir, I went 10 into the explanation how I did that yesterday. This was one of the assumptions that I assumed and is 12 stated further on at the end of this report, is that to 13 be able to do that I assumed that the digoxin, that 14 the digoxin like substances were derived from 15 digoxin. I see. 0. 16 And the assumption is worded 17 in my report. 18 I see. So, you simply treat, 0. 19 for these purposes, digoxin and digoxinlike 20 substances as digoxin? A. I assumed that the digoxin-21 like substances were derived from digoxin. 22 Right. And yet we have it,

Q.

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I gather from your evidence earlier this morning, that you weren't able to identify what those digoxin like substances were?

- A. That is correct.
- Q. Now, turning back to page 5 and the results of Allana Miller.
 - A. Yes.
- Q. And Note 2 on page 6 you say that the values or concentrations of digoxin in the heart or lung tissue were probably higher than Klotz solution. Did you attempt to calculate back from the measurement of the weight of the heart and lungs the range or possible concentration for digoxin in the heart and lungs in this case?
- A. I haven't done that because of the reason I have already stated in this instance about heart and lung organs were mixed.
 - Q. I see.
 - A. In that same container.
- Q. So, you only did that where there was either heart or lung but not mixed?
- A. Well, the heart mainly I believe it was, that's right, but only one, that's right.
 - Q. All right. Dealing with



Cimbura, cr.ex. (Roland)

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Estrella at page 6. You have estimated the level of digoxin in the heart at 55 nanograms per gram and we have seen that that is a low therapeutic level, in fact, it is the lower end of the therapeutic range that you have given us.

A. What I have estimated is not less than that.



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Q.	Yes.

A. That value by itself is quite low, yes.

Q Yes. Did you estimate what the highest possible range would be or could you do that?

A. Which chart are we on now,

Estrella?

Q. Yes. You have given the lowest.

Can you give an estimation of the highest?

A. No, I couldn't - there are so many complex factors involved.

Q. Yes.

A. That I reached a conclusion that I could not do it.

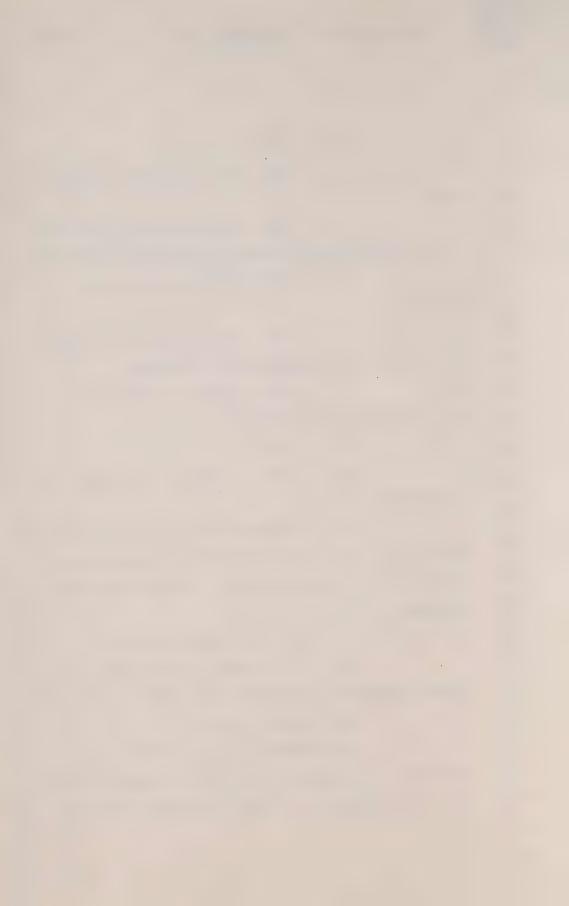
Q. Turning to the report of February 2nd, you have given us the results of analysis of a specimen from Allana Miller but it does not give us the value.

Is there any reason for that?

A. As I recall it, the value was already mentioned in the previous record. This is T29?

MR. LAMEK: Page 25.

THE WITNESS: Yes, I recall. In a sense what has happened there, sir, is when the first report was issued all we had time to do is the RIA



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MR. ROLAND: Q. Yes, I see it.

A. -- it is expressed as digoxin and/or digoxinlike.

Subsequently after I issued a report
we had an occasion to do the HPLC analysis as well, and
conclusions from that I have reported on the report
of February 5th. February 2nd, I am sorry.

Q. I have one last question about your report of April 6th. So I understand it, at the bottom of that report you have a note that an analysis of the sample shown in the note:

"... indicated the presence of
methyl alcohol and higher concentrations
of ethyl alcohol. These specimens
apparently did not contain any
preservative. Because of the unusually
high concentrations of ethyl alcohol
measured ... and because some of the
concentrations tended to increase with
time, it is suspected that these
findings are artefacts."

Now what are you referring to? Are you referring to the findings, the alcohol findings? You are not referring I take it to the dig. findings?



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A. No.

 $$\operatorname{MR.}$$ ROLAND: Thank you. Those are all the questions I have.

THE COMMISSIONER: Yes. Thank you.

Miss Kitely?

MS. KITELY: I will be ten or fifteen minutes, sir. Would it be appropriate to take a break?

THE COMMISSIONER: It would if you like.

Is that what you would like?

MS. KITELY: I would appreciate it.

THE COMMISSIONER: Yes. All right. We

will take 20 minutes now.

--- Short recess

--- On resuming:

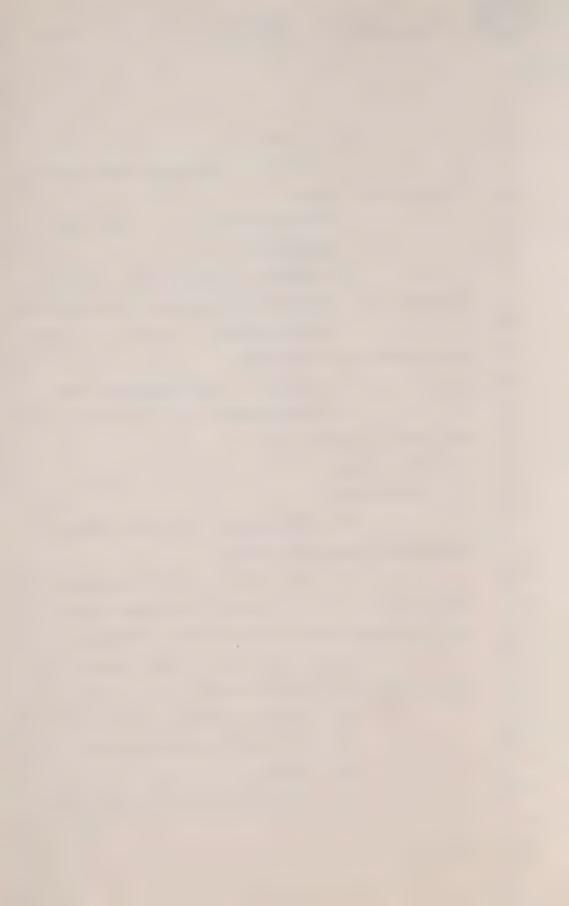
THE COMMISSIONER: Yes, Miss Kitely?

CROSS-EXAMINATION BY MS. KITELY:

Q. Mr. Cimbura, like Mr. Roland I too am interested in the ranges, and I want to deal with the ranges which you have shown in Exhibit 95.

Do you have a copy of that exhibit in front of you? That is your report.

- A. That is my report. Thank you.
- Q. On page 4 of Exhibit 95A --
- A. Yes.
- O. I would like to deal with Note 2





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which indicates a range for blood in fatal poisoning of 13.8 to 200. Right?

> Α. That is right.

Do you have a range for therapeutic for blood in serum?

> A. Do I have a range?

0. Yes.

A. As therapeutic?

If fatal starts at 13.8 --0.

Oh, I see. A.

Q. -- can we assume everything below that is therapeutic?

Well, according to research carried out at the Centre the range which I have attempted to illustrate is up to 12.4.

What happens --

Possibly up to 12.4. A.

What happens between 12.4 and 13.8?

Well, I am not sure I understand A.

your question as to what happens between there.

What I am getting at and maybe 0. it will be easier if we go to the next one which is the heart muscle, Note 3, and in that case you have two ranges. You have the therapeutic range which is 49 to 975, and you have the fatal range which is 108





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to 1240. Right? Are you with me?

TORONTO, ONTARIO

- A. At that time, that is right.
- Q. Well, we are dealing with your
- A. That is right.
- So you then start at 49 and carry on with the whole range up to 1240.

What is between 1 and 48? Just as in the blood what is between 1 and 13.8?

- A. Your question is clear but I am not really sure that I know what I should answer to it.
- Well, let's do it another way Q. then, Mr. Cimbura.
- A. These ranges are experimentally determined.
- Q. All right. But in each of the heart and the lung and over on page 7, Note 2, in the cases of liver, you have provided us with therapeutic ranges and fatal poisoning ranges.
- That is right. Based either on the research or on reported research, reported --
- Q. Exactly, but in the case of blood you have given us only the fatal, so I am interested to know what the therapeutic is for the blood?
 - For postmortem blood that is the



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range that I have given on one of the documents that you have seen yesterday.

Q. I just want to complete this absence - what appears to me to be an absence from the report.

Can you tell me how what figure I should be using for therapeutic for blood in conjunction with Exhibit 95?

A. Well, from my research in infants and children the highest - the range that I have found was between negative values and the highest value of 12.4 for children that were on therapy.

THE COMMISSIONER: A value of what did you say?

THE WITNESS: Pardon me?

THE COMMISSIONER: This value was what?

THE WITNESS: 12.4.

THE COMMISSIONER: 12.4?

THE WITNESS: That is what I have found

myself.

MR. HUNT: I am afraid I wasn't

following the question exactly but my friends at the table point out Note 1 on page 3 that may or may not relate to the question which is being asked.

MS. KITELY: Q. Well, have you got



Note 1 on page 3, Mr. Cimbura?

A. Yes.

Q. The difficulty I have with that, sir, is that therefore means there is a gap between 9.7 and 13.8.

A. There may be a gap, yes. Just no data experimentally produced in that.

Q. Well --

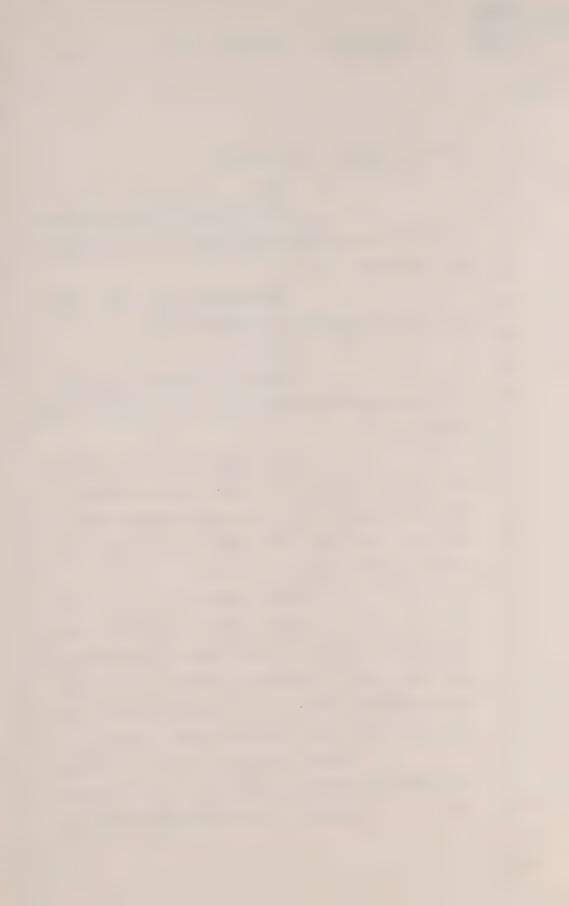
A. Usually in forensic toxicology work there is usually some sort of an overlap in these ranges.

Q. For purposes of what I want to do I am going to take the figure you just gave me which is negative or for my purposes zero to 12.4, and what I have done, Mr. Cimbura, and I don't know whether you can see it from here?

A. No, I cannot.

Q. Well, you won't need to. Well, no, because you have got your report in front of you and I just want to illustrate for the moment if we are dealing with blood, heart, lung and liver, you have got therapeutic and fatal ranges. Right?

I have now stuck in under therapeutic for blood and serum the range of zero to 12.4, and under fatal I have got 13.8 to 200 which would you





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agree	with	me	is	right	out	of	page	4	of	your	report
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A. Yes.

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TORONTO, ONTARIO

0. Under heart I have got under therapeutic 49 to 975.

> A. Yes.

And under fatal 108 to 1240 which is right out of page 4 of your report?

> A. Yes.

0. Under lung, 3.4 to 30 for therapeutic and 4.2 to 100 for fatal which is right out of page 4 of your report.

On liver I have got 2.1 to 190 under therapeutic and 35.3 to 580 for fatal which is right out of page 7 of your report.

Now are you with me so far?

A. Yes.

Okay. Now, as Mr. Roland pointed out there is a tremendous overlap between these ranges and so --

Between some of them. I am not A. sure if it is all of them, but some of them.

Well, I was going to use it as an example. Let's say you show a heart measurement of 100 - or, let's make it 125. All right. Now, that 125 falls at the low end of the therapeutic range and





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also at the low end of the fatal range so that one figure of 125 can be in either classification?

That is correct.

And to use another example with respect to lung, if we were to choose 5, then that is at the low end of the therapeutic range and also at the low end of the fatal?

- In blood, in postmortem blood. A.
- 0. In lung.
- Lung? Would you say that again?

The low end?

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- Your range is 3.4 to 30. 0.
- That is right. A.
- So if I am choosing 5 hypothetically. Q.
- Α. Yes.
- Then that is at the low end of the therapeutic and at the low end of the fatal?
 - That is right.
 - And whether you call it therapeutic 0.

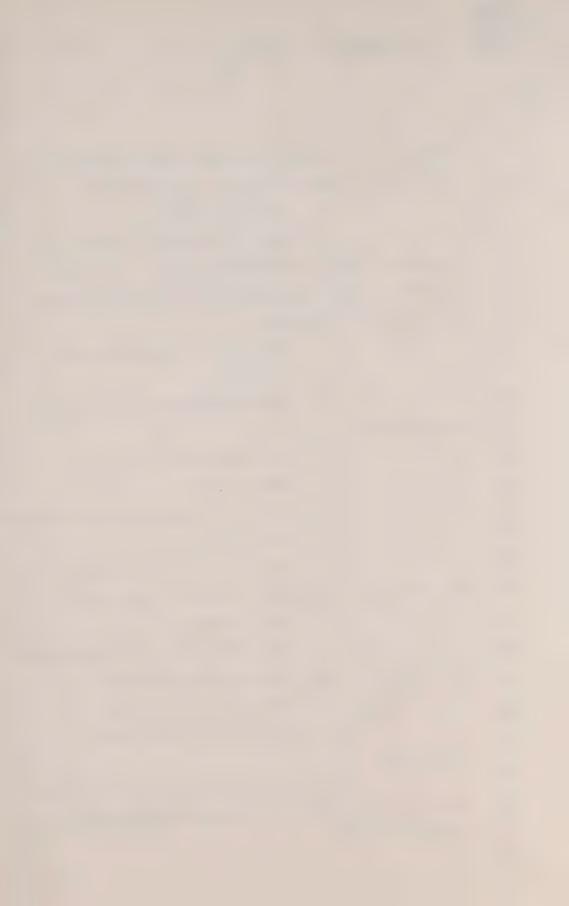
or fatal it is just a choice that one makes?

- No, it is not a choice.
- Well, it fits within both Q.

categories?

That is right, it fits into both, A. but it is not a choice. It is an experimentally

determined value.



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But it is the same 5, right, just using my 5 on lungs for now. Let's say your measurement says 5.

In one breath I can say that that is the fatal measurement and in the next breath I can say that that is a therapeutic measurement and I am right in both breaths?

> It fits --A.

THE COMMISSIONER: Except that one child died or at least one person apparently died from it and one who didn't.

MS. KITELY: I am talking about ranges.

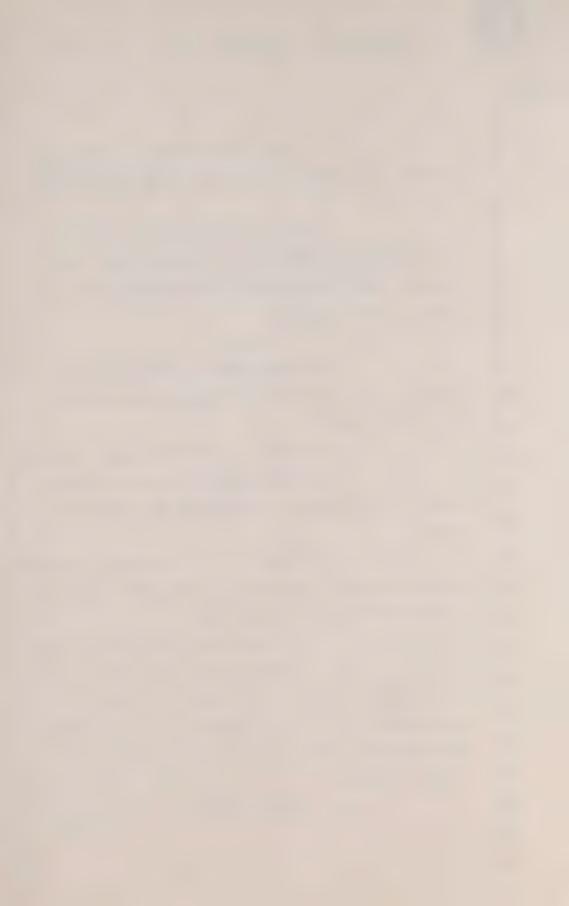
THE COMMISSIONER: Yes, you are quite right. I understand. I understand what you are saying.

MS. KITELY: Q. For purposes of plugging my hypothetical 5 I can plug it into either fatal or into therapeutic. Would you agree?

A. It fits into both, that is right.

It fits into both, yes. And if it is lung and if it is 3.1 it has to go into therapeutic. Or if it is lung and it is 35 it has to go into fatal. But I am talking about those overlapping figures.

> That is right. A.



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THE COMMISSIONER: It is the next step

trouble with it.

0. Right?

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A. There is an overlap.

0. So can we assume from this point that my hypothetical 5, it can go into either fatal for lung or therapeutic?

MR. HUNT: We can assume that only for the purpose of this discussion about the ranges.

MS. KITELY: Yes.

MR. HUNT: If my friend is going to take it farther which it sounds like she is with this reference to hypothetical, we have got to be sure that the very first step is just restricting that assumption to this discussion about ranges.

MS. KITELY: Everything I am talking about is in the context of ranges.

THE COMMISSIONER: I am entirely with you on everything you have said so far.

MS. KITELY: All right.

we are going to have trouble, but you go ahead. MS. KITELY: I hope we won't have

Now I don't think I got an answer from Mr. Cimbura although I did from Mr. Hunt.

THE COMMISSIONER: Can I answer, can



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I agree with you? No, you would rather have it from him?

MS. KITELY: I would rather have Mr. Cimbura agree with me if you don't mind, sir.

THE WITNESS: Your last reply was that 5 fits into either the therapeutic or the fatal range, that is right, it does.

MS. KITELY: Q. Okay. Now, let's go a little bit further. Would you agree with me in the context of your report not only did you examine each of those four but you examined bowel, stomach fluid, vitreous humor, chest fluid, right side, skin, brain and tongue. Would you agree with me?

A. Examined as part of the case, examination of the children under investigation? Is that what you are referring to?

Q. Yes. In 95 --

A. Not in my research, but you are referring to the children under investigation.

Q. I am only talking about 95, so, yes, the children under investigation, and I am suggesting to you, and quite frankly I have read your report, the other pieces of tissue that you looked at and the other fluid are those which I have just listed?

A. Yes.



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Q. Right. Would you agree with me? That I have examined other tissue

A.

Q.

other than what you have put on your paper there?

Yes.

A. Yes.



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	Ω.	Yet, and	d the only ranges th	hai
we have,	from what I	can tell	by Exhibit 95, are	
the four	ranges that	I put up	here.	

Α. Well, that is what you have, I may have additional information.

O. Well, just to satisfy me, am I correct that Exhibit 95 does not contain ranges for any of those other items?

> A. My report does not contain

Ω. Ranges for anything but those four.

A. Well, if you say so, I would have to go through it to refresh my memory.

Well to be fair to you, 0. Mr. Cimbura, the only place where there might be a range, and I say might be ---

A. I think there is one on skin there isn't there somewhere.

> Would you look at 95E? 0.

A. What page is that?

I don't know the page, it is. Q. the September 29th report, so it is the second last one.

A. Thank you.



 Ω . If you look at page 2.

A. That's right.

Ω. In Note 1 it reads that from the liver a fresh autopsy specimen, they were in certain ranges. But, if you look at those,
Mr. Cimbura, there are only three ranges there, the rest are just single figures; and so skin - would you agree with me --

A. Pardon me?

 Ω . Would you agree that on page 2 of the September 29th report, Note 1, there are seven items and only three of them have ranges?

A. Whenever there is more than one case there are ranges, that is right, for the single item there is only one case I based my conclusion on that.

 Ω . Well, looking at page 2 of 95E, the heart, you show one case and you show a range.

A. No, that wasn't meant to be - as I recall it in one literature report the value found in a poisoning range between 100 and 200 as I recall it.

 Ω . What I am trying to get at, Mr. Cimbura, we have got these ranges, blood, heart, liver and lung, right?



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A. Yes.

And my question to you is do 0. we have ranges for the other tissue that you looked at; you mentioned skin. Now if we look at Exhibit 95E.

> A. Yes.

0. You have a figure for skin but it is not a range.

No, because there is only one Α. case reported in the literature.

Right, so we don't have a Ω. range for skin, right?

> You say "we", including me? Α.

Q. I am saying this Commission at 11:45 on October the 20th doesn't have before it a range for skin.

A. Well, there may be ranges in the literature.

Are you equipped to tell us at this moment what the range would be?

> Α. For skin?

0. Yes.

If I could - I may have some Α. note in my notes if I could refresh my memory on that and perhaps I could tell you.



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0. Would you look.

THE COMMISSIONER: Well, what does this involve, are these present here, are you talking about - or have you something present here? THE WITNESS: I may have a summary

of values, sir.

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THE COMMISSIONER: Yes.

THE WITNESS: I am not sure if I have it with me or not.

MR. KITELY: Q. I have a simple way to do it, sir.

Α. As I recall the literature there is a therapeutic range for skin, not by work that I have done but by some other group, I don't recall the exact detail of the range.

Q. Mr. Cimbura, without having to pull your whole file apart, or whatever, I would like to do it in this fashion; we know we have four ranges.

> Α. That is correct.

And we know that there are 0. about six or seven other things that you looked at,

> A. Yes.

That we don't at our fingertips Ω . have ranges for. I mean you either have to look



through your file or go back to your office, neither of which I want you to do.

A. That's right I don't recall them right now but there are other ranges and some of them I may have available in my office, that's right.

Q. Well, we just want to get through evidence this morning so we are not going to get you to do that. We have four with ranges.

What I am going to ask you to do for the moment is to ignore those for which we don't have ranges and I will come to an illustration of that in a moment.

In your report you also refer to some substances, such as digoxin, embalming fluid and IV fluid, right?

A. It is mainly in the Klotz medium, yes, oh yes, in the Klotz fixed specimens?

Ω. No, I am talking about your separate examination of things such as embalming fluid, you did that on several occasions?

A. We analyze that by RIA, that's right.

 Ω . The point is that other than tissue and blood you analyzed certain products from the fluid in the IV line to the embalming fluid, is that right?



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A. That's right.

O. Now am I also correct from your evidence yesterday that where you have two values for the same piece of tissue, and one is on RIA and the other is on HPLC, that as far as you are concerned the HPLC is more reliable.

A. The HPLC result enhances my confidence in the RIA result.

 Ω . But having separated the material isn't it ---

A. The results are consistent.

O. But if the RIA said 100 and the HPLC said 80, didn't I understand you to say that you had more confidence in the 80 because of the separation process?

A. Yes, that's right with respect to certain specimens.

Q. All right.

A. That I had other information about as well for that.

MS. KITELY: Now, Mr. Commissioner, at the risk of being very tedious, and I am going to tell you where I am going before I do it.

I would like to review the report that is 95A through F, and I am going to ask Mr. Cimbura



to allocate with me the blood, heart, lung and liver specimens that we have in either therapeutic or fatal.

THE COMMISSIONER: This is a mathematical exercise, we can all do it, can we not?

MS. KITELY: Well, it is, and I have done it.

THE COMMISSIONER: Could you not just tell us what it is rather than have him go through this exercise if you have done it?

MS. KITELY: I can certainly do that, but before I do that I had best lay a couple more ground rules then.

THE COMMISSIONER: All right.

MS. KITELY: Q. Mr. Cimbura, can I ask you to go to Exhibit 95. Mr. Commissioner, perhaps what I will do if I can do the Cook child as an illustration of how I have done the mathematics for the rest.

THE COMMISSIONER: Yes, all right.

MR. HUNT: Does Mr. Cimbura have a

pencil?

MS. KITELY: He would probably like a pencil, yes.

 Ω . Now, because the information



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we had is, we have therapeutic and fatal, and because there are gaps; in other words, there is a gap between 12.4 and 13.8, I have established another little chart for purposes of classification. What this means is I am going to be classifying with you, if you will agree with me, under five categories; less than therapeutic; therapeutic; less than fatal; fatal; greater than fatal, and greater than fatal for example is 200 in blood. Are you with me, Mr. Cimbura?

Α. Less than therapeutic is below that range.

0. That was before you gave me 0 to 12.4 quite frankly.

> Α. Yes.

0. Now let's deal with Cook. So for example on T40 and T41 you show blood at 91 nanograms, and we are going to put that in the "fatal" category?

> Α. That is right.

0. The next is "tissue" at 1177, specimen T42 and we will put that in the "fatal" category.

> Α. For heart tissue?

Ω. Yes. The next is tissue from



the lung T43	at 153 and we are going to put that
	fatal" because the top of the range is
100; are you	

A. According to previously mentioned ranges this is a different range now.

 Ω_{\bullet} . I am talking about your report and the ranges that we have.

A. There is a different range now, I don't know what the point is.

O. Can we just follow this through, Mr. Cimbura?

A. Yes, okay.

On the next page under the "heart ventricle" Item TllA; now, as I indicated earlier where you have an RIA and HPLC, since you feel that the HPLC is more reliable I am relying on the HPLC figure. So to use the ventricle for an example, while you show 36 on your RIA you show 8 using HPLC. So I am taking that H from the ventricle and putting it right in the middle of therapeutic.

A. It doesn't make any sense at all, there is no range for that, there is a different range for that entirely.

MR. LAMEK: Fixed tissue.

MS. KITELY: Mr. Commissioner, I can



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only listen to one person at a time.

THE COMMISSIONER: I know, but the answer was, and I am trying to find out, there is no range, what did you say, Mr. Cimbura?

THE WITNESS: We are dealing now with fixed specimens.

> THE COMMISSIONER: Yes.

THE WITNESS: So whatever range there is is entirely different from fresh autopsy specimens.

THE COMMISSIONER: I see.

MS. KITELY: Q. All right. So that the range that we talked about, each of the ranges that we have here for heart, lung and liver are different from the range for - that we should use for the ventricle, is that what you are saying?

> Α. Ventricle fixed.

0. Fixed, yes.

Α. That's right, there is a different specimen, differently treated specimens.

Ω. I appreciate that, Mr. Cimbura.

THE COMMISSIONER: Let me get that

range, page?

MR. LAMEK: Page 4.

MS. KITELY: Ω . Now, the ranges

are on page 4, sir.



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THE COMMISSIONER: I take it that concentration in the heart muscle and those are fresh samples, is that it?

THE WITNESS: That is correct, sir.

MS. KITELY: Q. And this other one is - these are all, these were all in a plastic container and these were all in the solution, this Klotz solution is that it?

A: That is correct, sir. For those, any range you would have to use a range that I presented on the document yesterday, you remember that document for fixed tissue that I conducted a study and there is some sort of a range there.

 Ω . You mean Exhibit 213, is that what you mean, Mr. Cimbura?

A. I am not sure, if you will show it to me.

Q. Exhibit 213, is that what you are talking about?

A. No, the comparison of the ---

Ω. Are you talking about page 13

in Exhibit 213?

A. That is right. You see that gives you the findings that we found from hearts



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that had been placed into Klotz solution.

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- Ω . Are you saying on page 14 --
- A. Well those are just regions of the heart.
 - Q. Right.
- A. The first one would be more applicable for the range I suppose, if you wanted to combine a range you could combine them both I suppose.
- Ω . Well help me, Mr. Cimbura, these don't give ranges, they give numbers.

THE COMMISSIONER: To show the difference between Klotz fixed solution.

THE WITNESS: If you take the lowest from the highest you will have a range, I believe the highest is something like 11.

MS. KITLEY: Q. 11.0, yes.

- A. And the lowest I forget what it is.
 - Ω . Is 3.1?
 - A. Yes.
 - Q. Negative to 11.





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1 2 THE COMMISSIONER: What page are we on BB/cr now? 3 MR. KITELY: Page 13, Exhibit 213. 4 THE COMMISSIONER: Oh, the heart, the 5 region, oh, yes. Yes, 11 - negative to 11, yes, all 6 right. 7 MR. KITELY: Q. That negative to 11, 8 sir, that is the therapeutic range? 9 Α. That is obtained on children on therapy, that is a therapeutic range, that's 10 right. 11 Okay. Well then to go back 0. 12 to where I was on Cook, are you with me again on 13 page 2. 14 Α. Yes. 15 You've got PllA, ventricle Q. using HPLC, you've got the concentration of digoxin 16 was 8. 17 A. Yes. 18 Which we can put in the 19 therapeutic level because you have just told me that 20 the range is negative to 11? 21 Not really, you are comparing an 221 HPLC result with the ranges obtained by RIA. 23 Q. I appreciate that.



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Α.	So,	you	cannot	compare	the

- Q. Because No. 13 says RIA.
- Α. So, you cannot compare the two.
- So, we have no ranges for 0.

HPLC, is that what you are saying?

A. On Klotz fixed tissue, that's right. Well, there may be a range if you go through my report and combine whatever values are mentioned in there.

> Which report, 213 - Exhibit 0.

Α. Oh, my 95, I believe.

And you are saying that somewhere in 95 there might be ranges for fixed tissue using HPLC?

> That's right. A.

MS. KITELY: Well, Mr. Hunt, can you assist us, I haven't found it.

MR. HUNT: No, this wasn't my idea. I suppose the only way I could offer any assistance would be to suggest that some time may be taken outside of the witness stand where Miss Kitely can try and figure out these ranges.

THE COMMISSIONER: I wonder, Miss



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Kitely, if you can tell us what it is all leading to. What are you going to do. Just simply to tell us -- if the sole purpose is to say that there is no certainty about tissue measurements and that there is no certainty as to what they, speaking for themselves alone, what they indicate, as to whether the child has died of digoxin poisoning or not, I don't know that you would quarrel with that, would you, Mr. Cimbura. If you were given that tissue only, would you be able to tell from that test?

THE WITNESS: No, I wouldn't guarrel with that, sir, no.

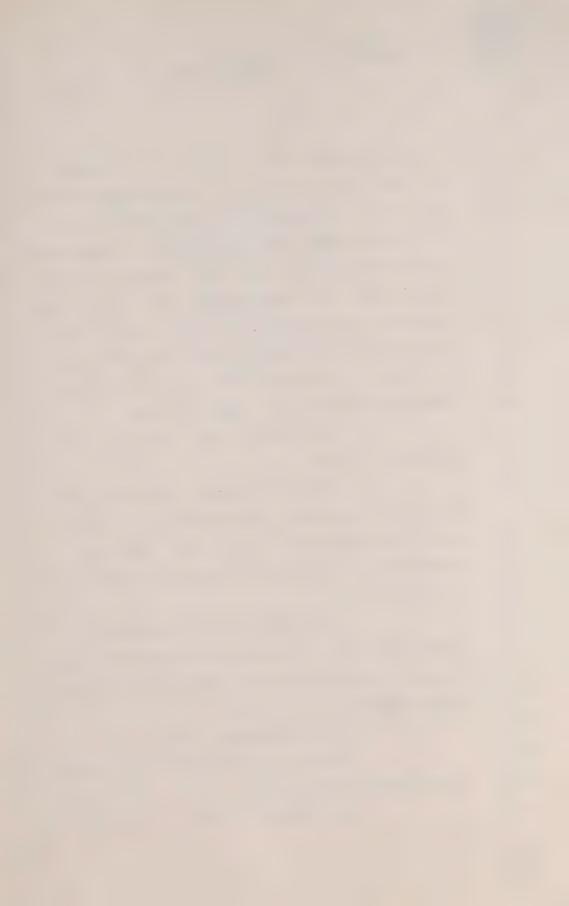
THE COMMISSIONER: Is that the point that you are seeking to establish because I don't think that anybody has claimed that. They are confirmatory at best of the blood test. Did I state it correctly?

THE WITNESS: That is correct, sir. Blood values are, I consider most significant tissues, fresh tissues as supportive evidence only. Fixed tissue is mainly inconclusive.

THE COMMISSIONER: Yes.

THE WITNESS: Embalmed tissues mainly inconclusive, that's right.

MS. KITELY: Q. Well, that wasn't



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exactly where I was going, sir. The direction of which I was going was to establish that there are by far a majority of the items referred to in Mr. Cimbura's report in the therapeutic range than in the fatal range.

What I suggest, sir, is because this information will become significant not so much with Mr. Cimbura, as I feel he is laying the ground work, but for the pharmocologists.

THE COMMISSIONER: Yes, but whatever it is, isn't it apparent without cross-examining him on it?

MS. KITELY: Well, except that it requires certain value judgments that I expected that he would want to reiterate. I am prepared not to flog the horse, sir, and I am quite content if Mr. Cimbura would be available so that I could work out this information so that I would have it for another witness. Then, I will leave the topic and get on with one of my friends for cross-examination.

THE COMMISSIONER: Well, I don't want you to leave it. If you have got something you want to prove I don't want you to leave it if you can only prove it by Mr. Cimbura.

But the report is there, is toxic



and non therapeutic ranges such as they are are there, but I think you have to be careful that you are not comparing, as the cliche has it, apples and oranges.

MS. KITELY: I agree, sir.

THE COMMISSIONER: Certainly a great many of these readings are in both therapeutic and toxic ranges, some of them are within the toxic range, some of them are within the therapeutic range. The real problem is that they don't prove an awful lot wherever they are.

MS. KITELY: I'm sorry I didn't hear you, sir.

THE COMMISSIONER: They don't prove a great deal wherever they are.

MS. KITELY: Well, it is something that I would like to sort out, sir.

THE COMMISSIONER: All right.

MS. KITELY: And long as I can take up Mr. Hunt's suggestion and meet with Mr. Cimbura to sort out these details I would be pleased to conclude my cross-examination because that's what I wanted to deal with.

THE COMMISSIONER: Is that possible that that could be arranged, Mr. Hunt?



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MR. HUNT: I think that's quite

THE COMMISSIONER: Yes, all right.

MS. KITELY: Thank you, sir.

THE COMMISSIONER: All right. Then,

Miss Jackman.

possible, yes.

CROSS-EXAMINATION BY MS. JACKMAN:

Mr. Commissioner, I think 0. Miss Kitely's direction in cross-examination was important and I would hope that if she can sort this out with Mr. Cimbura over lunch that it does go on record this afternoon because I myself was intending to follow up on some of the questions, we discussed it on break.

THE COMMISSIONER: Well, you had better get in on the conference. Would you like to get in on the conference?

MS. JACKMAN: Well, I think it is information that the other counsel should know as well.

THE COMMISSIONER: Well, no, no, but you get in on the conference and then if you want to, this afternoon - I don't know how we can do it. It is not for the purpose of supressing evidence it is for the purpose of some day getting out a



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report. I don't want to call witnesses back all the time and if it is possible, and I am not suggesting any impropriety that you have lunch with Mr. Cimbura or something like that, but if you do manage, if you don't mind to get it out of the way so that whatever has to be asked can be asked this afternoon

MS. JACKMAN: Yes, sir.

THE COMMISSIONER: So, on that basis, did you have some other questions you wanted to ask?

MS. JACKMAN: Most of my questions

follow from what Miss Kitely was going to ask.

and he won't have to come back, that's all.

THE COMMISSIONER: Well, why don't we put you and Miss Kitely on at the end of the show and see what has happened by that time and we will see.

Now, Mr. Olah, are all your questions along the same line too?

MR. OLAH: No, sir.

THE COMMISSIONER: Good.

MR. OLAH: May I volunteer then to

go next?

THE COMMISSIONER: Yes, all right.

MR. OLAH: Thank you.

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CROSS-EXAMINATION BY MR. OLAH:

THE COMMISSIONER: We have certainly almost without your consent or anything else we seem to be throwing you to the lions. Are you happy to give a little time to these ladies?

THE WITNESS: I would be happy. I had another commitment but I feel now that I should cancel the other commitment and I believe I will, I will do that.

> THE COMMISSIONER: Can you do that? THE WITNESS: Yes.

THE COMMISSIONER: Is it someone who will forgive you for that?

THE WITNESS: I am sure.

THE COMMISSIONER: Yes, all right.

MR. OLAH: Mr. Cimbura, I think you have already indicated this morning that the toxic range as far as you are aware of with respect to blood, and I take it that is from the literature, is from 13.8 nanograms per millilitre to 200 nanograms per millilitre. Is that the range?

Well, as far as I am aware of right now I have even found one a little lower value. That's the range I have used in my report.

> And that's the highest range Q.



(Olah)

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2	that's reported in the	literature?
3	Α.	The value of 200?
4	Q.	Yes, sir.
5	A.	Yes, up to 200.
	Q.	And have you ever experienced
6	yourself in your resear	cch anything higher than 200?
7	Α.	No, I haven't done research on
8	fatalities.	
9	Q.	Would it be surprising to
10	find a level, say, in t	the four, five hundred range,
11	would it surprise you?	
	Α.	Yes, it would surprise me to
12	some degree. It is hig	gher than what was reported
13	in the literature.	
14	Q.	Well, you do remember, do
15	you not, sir, that in	Exhibit 95-C you did in
16	fact report a level of	491 nanograms, did you not,
17	sir?	
18	MR. TOB	IAS: Which page?
	MR. OLA	H: It is 95-C. It is dated
19	March 25th,1982 and it	relates to the child Inwood.
20	Α.	My Item T46?
21	Q.	That's right, T46.
22	Α.	That's correct, sir, 491.
23	Q.	Are you surprised that your
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the result?

right.

HPLC and RIA combination there yielded a result of almost 500 nanograms?

A. Well, I am not surprised about the RIA and HPLC, I am not surprised about that.

Q. Well, are you surprised by

A. The result is 491, that's

Q. The question I have is, are you surprised by the result?

A. Well, it is higher than reported in the literature.

Q. Would that tend to suggest to you either some artefact or some error in yielding such a high result?

A. It's difficult to answer that because, you know, the literature reports, as far as I can recall, only about 9 in cases of fatal poisoning. So, that is a relatively small sample, there just haven't been that many poisonings by digoxin cases in children reported in the literature.

Q. Well, a few minutes ago when I asked you whether you would be surprised by a finding of over 200 you said you would be?

A. I said to some extent by the



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mere fact that it is above the reported fatal range, that's right.

0. Would you not agree with me, sir, that this result seems to suggest some sort of a deviation, either contamination or error to yield such a high result?

MR. HUNT: He has just answered the question, Mr. Commissioner. The very same question, it is difficult to say because of the fact the literature was based on so few cases.

THE COMMISSIONER: Yes, but I think the question now is, would this suggest to you that there might be some contamination that would cause that.

MR. HUNT: Well, the question that came before that suggested some error or artefact. Surely we are really dealing with the very same suggestion to the witness.

MR. OLAH: Well, I just want to get a clear answer so I know what this witness is saying.

THE COMMISSIONER: Well, I think it is all right, you go ahead, Mr. Olah.

MR. OLAH: Thank you.

0. Do you remember the question,

Mr. Cimbura?



again.

in testing?

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Α.	Would	you	mind	repeating	i

Q. Simply, the question was, does this very high level that we have here suggest that it is either an artefact or error in testing?

That it is either an error

0. Or an artefact or contamination

A. Or a artefact or contamination.

Again, I will say it is difficult to answer because perhaps you will have 50 cases of poisoning reported in the children it would be much clearer to answer that.

I see. So, your answer is you don't know, you can't say?

It makes one think of this possibility but I'm not really sure whether, you know, whether the possibility that there is something unusual, but I don't really believe that it suggests it by itself unless there is some other information available.

0. Okay. By the way, did you make - I assume when you did get this result you were surprised?

A. To the extent that it is higher



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2	than was reported.
3	Q. And I assume that you made
4	some enquiries in regards to that very unusual
5	finding?
6	A. Well, I'm not sure what you
	refer to as I made enquiries.
7	Q. Well, did you make enquiries
8	about the source of the sample?
9	A. I made at one stage or the
10	other. I'm not sure whether I made it at the beginn
11	or after, I'm not quite sure.
12	Q. All right. And your
13	information as to the source was that it was a post-
	mortem sample of serum?
14	A. That is correct. The source
15	of the information said that the serum was subjected
16	to - it was heated for a certain period of time at
17	a certain temperature, that's right.
18	Q. Do you know for what purpose
19	the serum was collected?
20	A. I don't know for sure.
	Q. Well, did you make enquiries?
21	A. I believe I may have made them
22	and I seem to recall some answer that it had to do

something with virology testing but I'm not sure

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or not.

yes.

whether my recollection is complete at that time.

Q. Would you have a note of that, Mr. Cimbura, somewhere?

A. I'm not sure whether I have

Q. Would you possibly check and let Mr. Hunt, your counsel, let us have the results of your search because, as you can appreciate, that is a fairly critical reading?

A. Oh, it is a very high reading,

Q. All right. Could you make those searches, please.

A. Well, I can, but you know, it is only based on reports. I think you should trace the source of the sample and let them decide who, where it was collected.

Q. You exactly anticipated my question of Mr. Lamek. Perhaps Mr. Lamek can assist us in that regard.

MR. LAMEK: I would do that merely to point to the Hospital. Maybe Mr. Roland can answer that.

MR.OLAH: I wonder who Mr. Roland is going to have to point to.



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MR. LAMEK: I don't know.

THE WITNESS: Well, I hope you

appreciate what ---

THE COMMISSIONER: It is information about the 491 but you didn't do the testing. You are on page, it is Exhibit 95-C, page 1?

MR. OLAH: Yes.

MR. ROLAND: Yes.

THE COMMISSIONER: And the reading is 491 and is on Kristin Inwood, blood.

MR. ROLAND: Yes. As I recall, Dr. Ellis did testify about a sample from Kristin Inwood that he did heat and this is, I presume, where Mr. Cimbura got his information.

THE WITNESS: Yes, that I have recorded, the heating I have recorded.

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MR. ROLAND: I can't recall now whether Dr. Ellis gave us a value for that sample of his testing or not, but I will look and see if I can find it.

MR. OLAH: It is not so much the value, I am interested in to know how the sample was taken, for what purpose, and when it was taken, so that we can establish what kind of a sample we are dealing with. It is a critical piece of evidence, Mr. Commissioner.

MR. LAMEK: My recollection,
Mr. Commissioner, and I think I can check this,
is that the sample was originally found in the
Hematology Department and therefore was presumably
drawn for some hematological purpose. Whether anyone
at this stage recalls the circumstances of the drawing
of the sample, I clearly do not, and perhaps in that
respect Mr. Roland could make enquiries.

MR. OLAH: I would be grateful.

MR. LAMEK: That is as much as I

can help my friend.

THE COMMISSIONER: The enquiry is about to take place, I think.

MR. OLAH: I am grateful for your help, Mr. Commissioner.



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Ω. A couple of other problems I had in going through your report, sir, if you would be good enough to turn to T40. That is Exhibit 95A which is on page 1. That is a blood sample as I understand it in which you got a result with respect to the Baby Cook 91 nanograms.

A. That is correct.

O. And as I understand it that was the sample that was forwarded by Dr. Cutz.

A. That is correct, sir.

Ω. And when the Hospital, as I understand it, tested that very same sample, turning to Exhibit 116, Mr. Commissioner, at page 57, my understanding is that their results resulted in a reading of in excess of 100.

Would the difference between those two readings --

THE COMMISSIONER: 116? Where do

MR. OLAH: Page 57, Exhibit 116.
That is the Cook chart.

As I recall that sample was taken at about 10:00 a.m. by Dr. Cutz and it is a sample from Pathology.

THE COMMISSIONER: Page 57?



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MR. OLAH: Clinical chemisty interim report, sir.

THE COMMISSIONER: Yes, I have it.

What column was it in?

MR. OLAH: It would be no time, sir.

THE COMMISSIONER: No time, and it

is the second column?

MR.OLAH: Second column.

THE COMMISSIONER: How do you know that is the same - I am sure that you are right but how do you know?

MR. OLAH: I think Dr. Cutz testified -

THE COMMISSIONER: That it was the

same one?

MR. OLAH: Yes, because you will recall that the autopsy was performed that morning and started I think around 9:30 or 10 o'clock, and you will see all of the samples are taken earlier than 10 o'clock.

THE COMMISSIONER: Well, I have no doubt you are right, but why do you concentrate on that one, D57978? Is it because of something Dr. Ellis said?

MR. OLAH: I am concentrating on it because it is the very same sample as tested



T4

at the Hospital for Sick Children, and it was tested by the Centre.

THE COMMISSIONER: I am being a little dense. How do you know it is the same sample?

MR. OLAH: Well, as I understand it,
Dr. Cutz at autopsy --

THE COMMISSIONER: Yes.

MR. OLAH: -- took some sample of blood which was then analyzed.

THE COMMISSIONER: And so it is because of the reference to Dr. Cutz?

MR. OLAH: That is correct, sir.

THE COMMISSIONER: Now is the one that he took, which is the second column on page 57, has that been established it is the one he took?

MR. OLAH: I believe that is what the evidence indicated. That is my recollection. But no matter which sample we take, whether it is column 2, 3 or 4 you will see that there is disparity between those readings and the readings taken at the Centre.

All I am trying to ascertain is whether the difference for that or the explanation is because Mr. Cimbura was using HPLC in combination



with RIA, whereas I believe the Hospital was simply using RIA. I just want to understand why there are different readings for what appears to be the same sample of blood.

MR. HUNT: My only concern is that if that is the question - and I see my friend's problem - we have to know precisely whether it is the same sample. There is no point in asking Mr. Cimbura to comment on that precise question unless we have it verified by the evidence of Dr. Cutz that it is the same.

THE COMMISSIONER: Well, we may have had that; I just don't remember it. I was hoping that Mr. Olah could point to something that would identify which one - in any one of these cases there is a difference.

MR. OLAH: Yes, and all I want to know is why one institution gets one reading and why the other institution gets a different reading.

THE COMMISSIONER: I would just like to assume, though, that it is one of those three, that is all.

MR. OLAH: I believe it is, and perhaps I can put in a hypothetical and come back -THE COMMISSIONER: All right.



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MR. OLAH: -- some other day and point to the transcript reference if you like, Mr. Commissioner.

THE COMMISSIONER: All right.

MR. OLAH: I am being given

instructions by the television crew.

THE COMMISSIONER: What are you

doing wrong?

MR. OLAH: I am speaking too close

to the mike.

THE COMMISSIONER: You can't say we don't learn something every day.

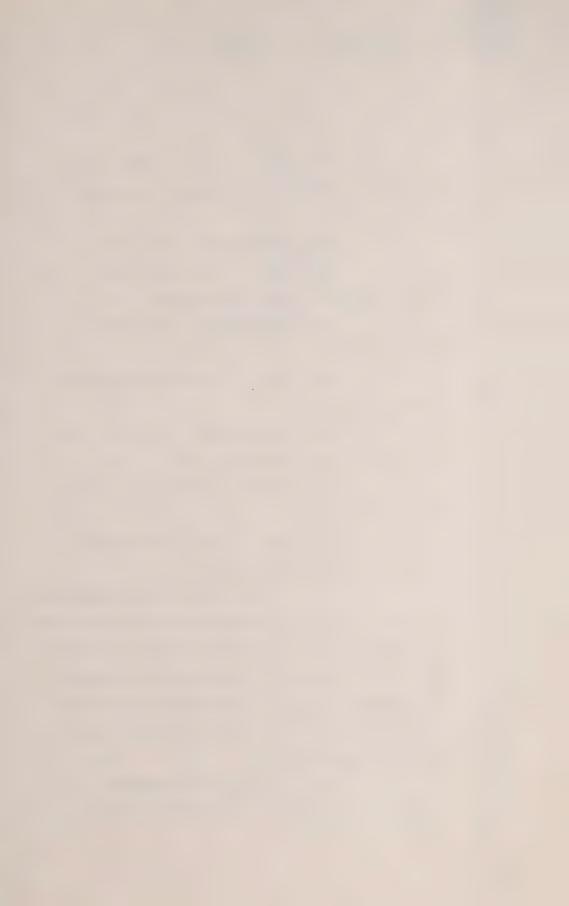
MR. TOBIAS: He will never make it in show business.

MR. OLAH: I will have to take acting lessons next, Mr. Commissioner.

Mr. Cimbura, do you understand my concern and can you perhaps assist me as to what explanation if any, assuming that those are the same blood, that is taken at the same time, is there some explanation that you can offer us as to why we are getting different readings on what appears to be the same blood.

A. What is the reading?

MR. HUNT: May we also just point



J7

out so that my friend doesn't have to go over it,

Note 6 on page 4, Dr. Wong's test was run on

sample T41 which is also part of that two samples

my friend is referring to, and Mr. Cimbura has

already indicated his reading was 100 on his

analysis of that sample, so that maybe with respect

to this particular sample we have three readings

from three different sources.

MR. OLAH: Well that makes it even more interesting.

MR. LAMEK: Well, there is one other thing, with respect, Mr. Commissioner: it is clear on the evidence that although we do not know what RIA kit the TGH uses we do know the one used at the Sick Children's Hospital is different from the one used in the Centre for Forensic Science.

In order for my friend to expect absolute identity of result he must surely posit the same equipment, the same procedure, absolute similarity or identity all the way through.

MR. OLAH: Well, that may be the answer, and if Mr. Cimbura can give that answer I would be grateful.

All I am seeking: we seem to have in several cases like, Mr. Commissioner, you will



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recall that one result went to Mount Sinai Hospital on Pacsai.

THE COMMISSIONER: Yes.

MR. OLAH: Resulted in 26 at Sick Children's and resulted in something like 120 at Mount Sinai.

What I want to explore is how certain can we be with respect to RIA results when we are getting those kinds of discrepancies? And certainly I would assume that is a proper question.

question. That last comment, though, is argument.

It is not a question at all.

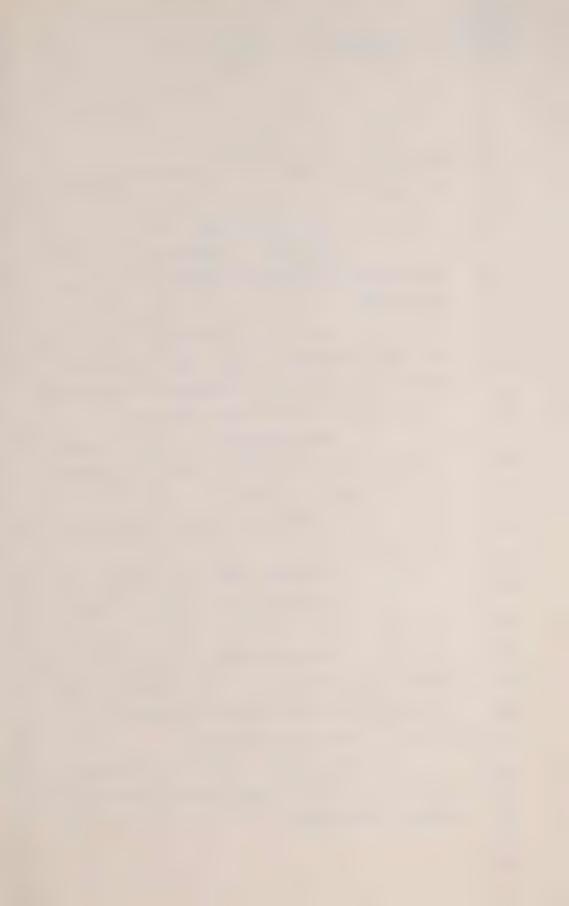
MR. OLAH: I am just trying to point the direction --

THE COMMISSIONER: All right.

MR. OLAH: -- so that my friends appreciate where I am going.

THE COMMISSIONER: All right. If it is one of the three on page 57 of Exhibit 116, and if that is also represented by T40 and T41 in Exhibit 95A there is a discrepancy.

MR. OLAH: If there is a concern about it I can go to a sample which is identical and show a discrepancy.



that way.

.T1 0

THE COMMISSIONER: Yes. All right.

MR. OLAH: Perhaps I should do it

THE COMMISSIONER: I was just giving you a preface. Now you ask the question, can you account for the discrepancy? Isn't that the question you want to ask?

MR. OLAH: That is the question I was trying to ask and I am grateful for your assistance.

Q. Do you understand the problem or the concern I have, Mr. Cimbura?

A. I understand your concern. I am not familiar with this document so I am not sure what value you want me to compare.

Q. Well, in one case assuming that we have got the same blood, we have got a result of in excess of 100 nanograms. We don't know how far. It could be 200, it could be 300, or it could be 101.

Assuming that the blood was taken the same time, your results would seem to indicate a reading of 91 nanograms.

- A. It so indicated.
- Q. Which would indicate at least



a 10% difference between the two readings. Can you assist us as to why we would get that kind of a difference?

A. Well, I think a difference of 10% between our degrees would not be bad if it was 10%. Some reasons that may be responsible for that is the reason Mr. Lamek mentioned. Another reason is that our method, as you know, uses extraction where you expect to lose something so it has a tendency to lower results to some degree.

Q. Let's go on to the case that I posited to - or we have had in evidence already here, where the Pacsai reading at the Hospital for Sick Children was 26 nanograms, and the one that was obtained at Mount Sinai using an RIA method was somewhere in the order of about 112 as I recall.

impossible for him to answer. Those are two entirely different institutions.

MR. OLAH: If I may be permitted -THE COMMISSIONER: Yes, but that
he had no part of.

MR. OLAH: Q. Would that kind of a range be surprising to you or is that kind of a variation that is something to be expected?

A. If it was done by the same RIA



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it would be surprising and you would not expect it by the same procedure.

 Ω . Would simply the difference in kit, would that result in that kind of variation in your experience?

A. I wouldn't think in that kind of a variation, no.

Q. What kind of a variation should we be expecting in your opinion, Mr. Cimbura, assuming a different kit and perhaps an extraction process being added to the RIA as opposed to an RIA alone?

THE COMMISSIONER: We had a chart on this somewhere at some point way back when, in which somebody experimented with --

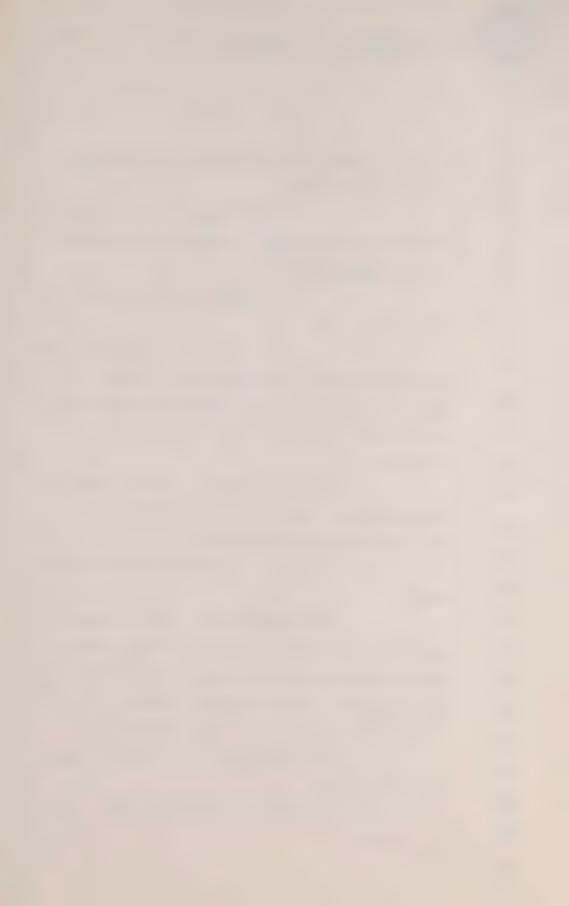
MR. OLAH: With the different antibodies.

it was somebody experimented with certain testing done by various institutions under RIA and HPLC and everything else. Did you produce that?

THE WITNESS: No, I haven't.

THE COMMISSIONER: I thought it was early, very early.

MR. LAMEK: It may have been Dr. Seccombe.



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THE COMMISSIONER: It might have

MR. OLAH: There was Exhibit 8 in which they got half the readings in one instance using a different antibody or using a different kit. That is the report --

THE COMMISSIONER: I won't take up everybody's time but I know that we have had that and it shows variations and it shows - it is a chart of some sort and it may have been in one of the reports. They had the various institutions throughout North America doing it.

Well, I would be wasting a lot of time looking for it now, but I know there is such a thing. It doesn't matter, so you go ahead with your questions. I know we did have that chart from somebody.

MR. OLAH: Q. Going back to something else that was explored with you this morning, Mr. Cimbura, you will recall when you were examined by Mr. Roland about the analysis of postmortem blood in heart tissue from children not on digoxin therapy (that is page 8 of Exhibit 213), in the 12 samples of children under two months that were tested there was no digoxin recorded by the RIA alone.



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Is that your evidence, sir?

A. Document 8, is it, Exhibit 8?

MR. LAMEK: Yes.

THE WITNESS: That is right, 24

children were analyzed.

MR. OLAH: $\ \ \mbox{$\Omega$}.$ And 12 of those were two months or less?

A. That is right. The results of the RIA analyses gave a negative result.

Q. I assume you have read the literature that has been filed as exhibits in these proceedings and you are familiar with the various reports such as the New England Journal Report, the Waldous Report, the Brett Report and all of the other findings in which simple or RIA alone in babies, applied to baby's blood, found a digoxin-like substance. In other words, recorded something that wasn't digoxin because the children didn't have digoxin given to them.

A. I am not sure whether I am familiar with all of the reports you mentioned, but I am familiar with this phenomenon, that is right.

Q. Well, that was the experience of the Hospital for Sick Children you will recall. Are you aware of that, that digoxin was found in



children who were not supposed to have received digoxin. That was on another floor.

THE COMMISSIONER: On the 7th floor? $\mbox{MR. OLAH:} \quad \Omega. \quad \mbox{On 7C and D. Were}$ you aware of that, Mr. Cimbura?

A. I am not aware if I am or not because we have had so many phone calls throughout the years that I think I was aware to the extent that they thought at that time they had values where they shouldn't have had values, that is right.

Page 1863 follows....



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You are aware of Dr. Seccombe's 0. works and his evidence, are you, about the finding of digoxinlike substances?

Yes, I read his brief paper a long time ago, several months ago.

I guess what I am curious about, sir, why is it that in all of these reports when an RIA technique is applied in situations where patients don't have digoxin, and they find a digoxinlike substance, when you apply your RIA to patients not on digoxin you don't find those kind of digoxinlike substances?

Well, as was mentioned before by negatives means a detection of less than 1. That may be a partial answer. Another answer may be that none of these investigators as far as I am aware have used an extraction prior to the RIA.

O. Excuse me, sir, if you have a look at Note 1, it seems to indicate that the process of analysis was by radioimmunoassay method, does that mean it was HPLC in combination with RIA, or just RIA alone?

A. Well, RIA to which extraction was applied before RIA, that is the procedure described, I see. So you are saying that



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the	extraction	may	have	removed	this	digoxinlike
subs	stance?					

I have no proof, but it may, that A. is right.

And if it doesn't, then what 0. other explanation could be given for the fact that approximately six other teams have found this substance when applying RIA, and some of them have found fairly high readings within the therapeutic levels; whereas you did not find that digoxinlike substance?

MR. HUNT: Let my friend in addition put to the doctor ---

MR. OLAH: I am sorry, he is not a doctor.

MR. HUNT: I am sorry, to Mr. Cimbura, and thank you for pointing that out, Mr. Olah. Let my friend put in addition the evidence of Dr. Seccombe with respect to the kit that he was using and his findings insofar as the kit and its reactivity with the substance was concerned, he left that out of his presentation.

MR. OLAH: O. I think in all fairness, Mr. Cimbura, the kit, depending on the kit you used you find different values, and if that is the answer for why you didn't find this digoxinlike substance,



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All I am interested in is why six teams seemed to have this experience and your team doesn't seem to have that same experience?

A. I think I am giving you the possibilities.

THE COMMISSIONER: Yes.

MR. YOUNG: I hesitate to interrupt my friend, but my recollection of Dr. Seccombe's evidence was a little more than that. He said that the particular assay, the antibody used in this particular assay seemed to cross-react in a very different manner than any other antibody that he had come across. He went to great lengths and brought up all the antibodies he could find that would react in this way and he thought this was an unusual reaction, and indeed that would probably explain the distinction.

Might I also point out while I am standing, Mr. Commissioner, I think the chart that we were discussing earlier is in Exhibit 25, on the last page there is a ---

> THE COMMISSIONER: 25?

MR. YOUNG: It is a chart that seems to compare RIA and TDX and results of various hospitals and institutions.

THE COMMISSIONER: That is the one I had in mind.



MR. YOUNG: Is that the one?

THE COMMISSIONER: Yes, I think so, thank you, Mr. Young.

MR. OLAH: In all fairness, in response to Mr. Young, Mr. Commissioner, Exhibit 8 is a case in which two different antibodies were used and in both instances digoxinlike substances were found although in different quantities. So that simply to suggest that only in one RIA antibody do you get this kind of phenomena is not quite so.

THE COMMISSIONER: Well, we are getting into argument several months ahead of time.

MR. OLAH: Yes, sir.

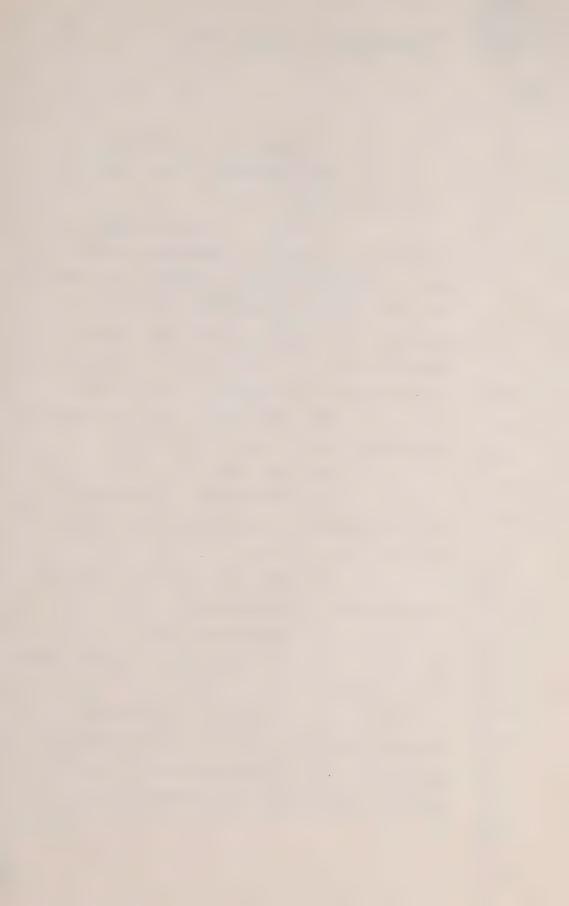
THE COMMISSIONER: No, that is not the one I had in mind, Mr. Young, it is not 25, there is another and I will find it.

MR. OLAH: May I then put my question to the witness, Mr. Commissioner?

THE COMMISSIONER: Yes.

Q. Mr. Cimbura, can you then respond to that problem?

A. I believe I have partially responded, there are differences between methods, our method employs an extraction which sort of purifies the blood before the RIA. Our method ---



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(). May I stop you there, you are then suggesting that your extraction process takes out this Substance X or whatever it is?

MR. HUNT: Would you please let the witness finish. You should not interrupt him and then say, that is what you mean to say.

MR. OLAH: I was simply following up on one portion of the answer, Mr. Commissioner.

MR. HUNT: That is not what my friend was doing, Mr. Commissioner, he was stopping the witness part way through the answer and saying, there, that is the answer.

MR. OLAH: Well, if that is not correct I am sure --

THE COMMISSIONER: Try the question again then, Mr. Olah, and we will see what happens. I know it is a long question, but you know what the question is, we have had it now four or five times. Can you account for the differences in the results between your method and other people's methods, and we will try and let you go at least until 1 o'clock and then --

MR. OLAH: With Mr. Hunt's help I am sure we could go longer.

THE COMMISSIONER: Could you try that



one again now, start at the beginning.

THE WITNESS: I understand the question is: why are we not seeing any Substance X as compared to some of the reports and the literature?

MR. OLAH: That is precisely the question.

THE COMMISSIONER: Yes.

THE WITNESS: As I said that possibilities, one of the possibilities is that we are using extraction which may remove Substance X. Another possibility is that as far as I am aware I have not seen the same antibody, the same manufactured kit that was used in the literature that was published, and here this is, to the best of my recollection, I may not have seen them all, but certainly the one by Dr. Seccombe did not include the same antibody that we had used.

Another partial explanation may be that our detection limit is a little bit higher than was — I believe Dr. Seccombe wanted to see, apparently was as low as .2 or something like that, I don't recall.

MR. OLAH: Q. Let's take those step by step. You are saying then that the extraction process is far - possibly takes out Substance X?

A. It may, I have no proof of that



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is the reason why I extract or remove certain things that I don't want in the test.

Q. And that is the separation technique, is it, sir?

but it stands logically for a person in my field that

A. That is extraction technique; whereas blood is extracted with some solvent, organic solvent. So in effect you are transferring the digoxin from the blood, from the mixture, you know how blood looks red and so on, into the organic solvent which is much cleaner after that time.

Q. When you were carrying out this study were you aware of Substance X at that time?

A. I don't believe I was then but

I was aware of the general limitations of IRA and the caution to purify blood before apply tests.

Q. So would it be fair to say that other than sort of the general attempt to purify the blood you were not specifically to exclude Substance X?

A. Well, I believe at that time there was no mention specifically of Substance X anywhere.

Q. And your detection level was from 1 nanogram up, was it not?

A. That is right, the detection



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level negative means that it is ---

It is 1 nanogram or --0.

That it is less than 1 nanogram.

Less than 1 nanogram?

If it is that, because you don't know, it is negative.

MR. OLAH: I am about to traverse to a different area, Mr. Commissioner.

THE COMMISSIONER: Yes, all right.

MR. OLAH: Thank you.

THE COMMISSIONER: For your benefit,

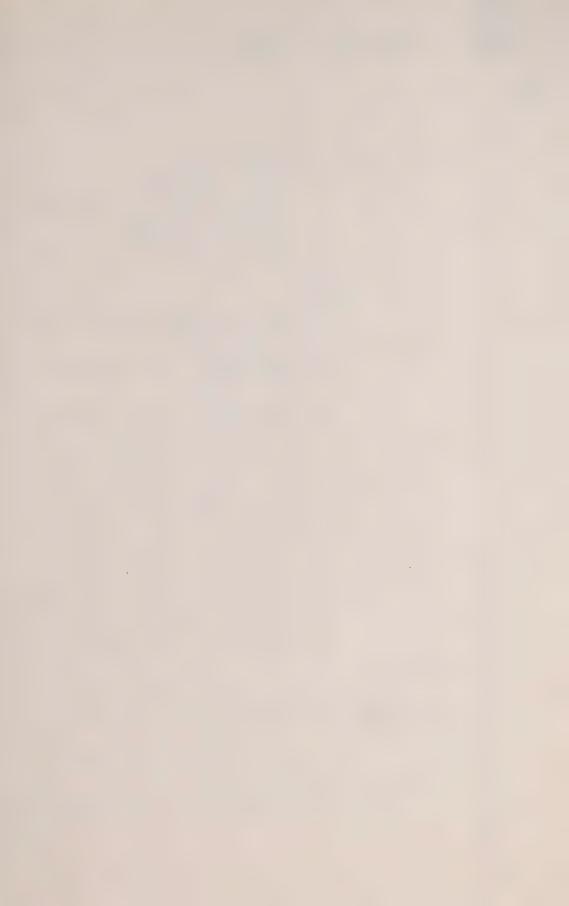
Mr. Lamek, it doesn't look as though we will be able to take on anyone else. I would like to say that I am anxious to complete Mr. Cimbura today. So it is possible we may be sitting a bit late. If we do manage to get through before 4:30 I won't hold it against you that you don't have anybody standing by.

MR. LAMEK: All right, thank you.

THE COMMISSIONER: All right then,

two-thirty.

--- Luncheon adjournment.



A/	'BB	/a	k

--- Upon resuming at 2:30 p.m.

THE COMMISSIONER: Yes, Mr. Olah.

MR. OLAH: Thank you, Mr. Commissioner.

Ω. Mr. Cimbura, I'd like to now change the focus of our discussion to some other matters that were of concern to me. I'd like to have you turn if you could to Exhibit 95A, please. That is your initial report, sir. In particular, if I could ask you to turn just as a matter of example to page 4, T7.

A. Yes, sir.

 Ω . As I understand it, the RIA alone yielded a result of 242 nanograms of digoxin and digoxin-like substances.

A. That is correct, sir.

Q. And then subsequently with the more refined test.

A. You are referring to the left ventricle of the heart.

Q. Yes, left ventricle.

A. Yes.

Q. When you combined the HPLC and the RIA you got a pure reading or what appeared to be a pure reading of digoxin at a 105 level?

A. That is correct, sir.

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	Q.	In other	words, we	can	say
with some	degree of	certainty t	hat there	was	
ıpproximat	cely 119 na	nograms of	digoxin-li	ke	
substance	in the sam	ple you tes	ted. That	is	digoxin-
ike subst	ance as op	posed to di	goxin.		

A. No, the total value for the digoxin and digoxin-like was 242.

 Ω . Well, if I segregate out the digoxin alone would I not be left with digoxin-like substances?

A. Well, it appears to make sense but I'm not sure whether one could make that deduction because of the different reactivities of whatever these digoxin-like substances are present there.

about precise numbers. What I'm trying to get is a rough estimate or a rough weighing of how much digoxin-like substances there would have been in that particular sample for a question I want to pose to you after that. Would it be fair to say that it was a fairly large amount of digoxin-like substance?

A. Yes, it was relatively high, I would agree, yes.

Q. And the question I really



wanted to get at was this. I don't know if you can assist me in this regard but would the digoxin-like substances come from the breakdown of digoxin?

A. That was my conclusion that they were derived from digoxin.

 Ω . And that breakdown, as I understand it, is a result of the tissue decaying or digoxin being released from the tissue?

A. No. Actually, what I believe is that the chemicals in the Klotz solution - the Klotz solution consists of various chemicals and a combination of these chemicals - well, either one or a combination of these chemicals chemically degradates digoxin to digoxin-like substances.

Q. All right. So, the mode is different, or the mechanism. But the point I'm trying to ascertain is this. Would it be fair to conclude that at some prior time, some time prior to the measurement that you obtained, the digoxin level would have been substantially higher than the 105 nanograms recorded in your result?

A. There is a possibility that it was higher, that's right. If the analyses was carried out at some time prior to that time.

Q. And I guess there is no way



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of quantifying how much higher that reading would have been, say, at the time of death as opposed to whenever you took this actual reading?

A. That was the conclusion I reached after examining all the multiple factors that complicate this issue.

Q. Can you assist us as to whether it would be substantially higher or marginally higher?

- A. It would likely be higher.
- Ω . All right.
- A. It could be substantially higher but of course I don't know, I cannot give you any figure.
 - Q. All right.
- A. The only figure I could give, and the figures where I have expressed as a minimum concentration in the fresh heart in some of the specimens.
- Ω . I'm sorry, where you expressed it as a minimum?
- A. Minimum concentrations of digoxin in the fresh heart before fixing.
 - Ω . I see.
 - A. In my opinion that was the



only estimation that I could reach from all these figures.

Ω. Well, would it be fair to say that tissue in preservative over some period of time, if it had been brought to you, hypothetically, fresh, it would have been higher than the figures we see listed here?

A. You mean if it was brought to me in Klotz medium but relatively soon after it was placed in it?

Q. Correct, correct.

A. Yes, I would expect the figures to be higher, that's right.

 Ω . All right.

A. Depending of course just - it would depend. If I received those specimens immediately, for example, after they were placed into the Klotz solution, then of course I could believe that the concentrations in the heart tissue then would be of a similar magnitude as they would be in the fresh tissue because some time is needed for the digoxin to diffuse into the tissue, into the surrounding medium and also some time is required for the chemical degradation of digoxin.

Q. From your reports or your



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studies I noticed that you experimented with respect to the degradation of digoxin in preservative fluid. Did you have any opportunity to measure what the degradation is with respect to tissue or different kinds of tissue in Klotz solution?

- A. Yes, those were two documents that were presented yesterday.
- Ω. All right. I would like to now discuss another area with you and, in particular, I'd like to refer you to Exhibit 95E. It is the report September 25th at page 5. In particular, I would like to refer you to Laura Woodcock.
 - A. Yes, sir.
- Ω. On tissue analysis with respect to that child. At the time that you did these tests, or thereafter, did you ascertain or make any enquiries as to whether some of these children did not receive digoxin during their life?
 - A. I believe I have, yes.
- Q. And was Laura Woodcock one of those children?
- A. Well, based on my recollection she did receive some digoxin some time before her death.
 - Q. All right. And would this



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account for the traces of digoxin found in her system or in the tissue that was analyzed? You will see that T103 refers to a trace, very low levels, in other words.

- A. That's right.
- Of digoxin-like material. 0.
- Α. Yes.
- Ω. Did you make enquiries with respect to the children Lombardo, Belanger and Hines to ascertain that at no time during their life were they on digoxin?
- This information was provided A. to me, yes.
- Q. What were your expectations in running tissue sample studies, and I quess we have to segregate Hines and Lombardo and Belanger because they were different kinds of samples, but dealing with Belanger and Lombardo, what kind of expectations did you have in terms of digoxin results?
- A forensic toxicologist doesn't have any expectations.
 - All right. 0.
- It is an unknown situation A. and you analyze it and report what you find.
 - Q. All right. Once you received





those reports w	ith digoxin,	certainly	with	respect
to the Lombardo	child, being	found in	some	of the
exhumed tissue,	were you sur	prised?		

- A. It was a finding which was contrary to the history available about the child, that's right.
- Q. All right. In other words, in retrospect, would you have expected to find either a trace or no trace of digoxin in those tissues?
- A. Well, if the child Lombardo was not given digoxin I would expect to find nothing, no digoxin in these tissues.
- Ω . Now, I want to be clear with respect to those two children. They were exhumed tissues?
 - A. Right.
- Q. And is it the combination of the RIA and the mass spec. that gives you some confidence if any in the results from those tissues?
- A. Well, the confidence that one obtains in my field of work is from experience, long experience dealing with examination of drugs in body specimens and of course the results of the tests that one obtains. The confidence that I have,



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that I have reported, constitutes a conclusion made at the end of all of the analyses that were made.

- Ω . Fair enough. Now, as I understand your conclusions your major conclusion is that you cannot really help us in terms of the actual levels in the tissues of those two children?
 - A. Which children?
- Ω . We are talking about Lombardo and Belanger, the exhumed tissues.
- A. Well, I think they have to be separated for consideration. Generally speaking, essentially at the later stages of the investigation, the results in tissues of exhumed children I considered inconclusive with respect to digoxin toxicity.
 - Q. All right.
- A. The Lombardo child, while he falls into this category, had substantial amounts of digoxin. That is I think the best I can say.

 The amounts found in his tissues were higher than all the other exhumation cases.



BB EMT/cr Q. Yes.

A. The results are still by themselves inconclusive and with respect to digoxin toxicity, however.

Q. I would like to turn you to the note on page 4 of that particular report which reports on the child Belanger, Note 3, and I take it that ---

A. Which page is that, sir?

Q. Page 4, Note 3, about a third of the way down the page.

A. Page 4, Note 3?

O. Yes.

A. And that is the note - I will just refresh my memory.

O. Please take a moment.

A. That is the note with respect to child Belanger, is that right? Yes, sir.

Q. I guess what you are saying there is that the extent of the digoxin concentration cannot be ascertained with a degree of scientific certainty, but my question is certainly you have no doubt that digoxin was found in those samples? That can be ascertained with a reasonable degree of scientific certainty?



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quantitative	interpret	atio	ons;	you	said	l based	l on
numbers.							

Q. Right. But you have no doubt today as to the fact there is a reasonable scientific certainty, you can say that to the Commissioner, that in fact digoxin was found in those tissues?

Α. That is correct, sir, within what I call a reasonable scientific certainty I believe that we found digoxin in these tissues.

0. That is the distinction I wanted to clarify.

I take it you make the same observation with respect to the Lobardo child?

A. A similar observation with the qualification, as I said previously, that in child Lombardo the amounts found were substantial.

Q. Yes.

I still cannot conclude from that alone on digoxin toxicity, but the fact remains that they were substantially higher than all the other exhumations - childs exhumed.

Q. All right.

I would like to go back to the child we started our discussion with, that is the child





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ranges.

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Inwood. I notice in Exhibit 95A - that is the first report - at page 8 you conclude that ---

A. I am sorry, oh, yes, page 8, is it? Yes.

Q. - that an estimate of the concentration of digoxin in the heart before it was fixed in the Klotz solution was not less than 549 nanograms per gram?

A. That is correct, sir.

Q. And do I take that to be in the toxic range as well as the therapeutic range?

A. That is right, it is in both

Q. All right. Now you remember that you and I talked about the serum when we first started our discussion, and that was a very, very high reading in the toxic range? Correct?

A. In serum from?

Q. In serum.

A. From the same child?

Q. The same child.

A. Yes. A value you are referring

to is 491 that was found?

Q. That is correct.

A. That is right. It was above



the fatal range.

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Q. All right. Now you remember Miss Kitely saying to you that where you have got a tissue sample falling into ranges, it is difficult to ascertain whether it is in a therapeutic range or the toxic range. Do you remember that? Do you remember that discussion?

The discussion I have is bearing in mind the serum reading in this case which was very high, does that assist you in determining whether in fact this child was administered toxic doses of digoxin, or can you assist us in that regard?

To go back first to the finding under my Item No. T8 from the child Inwood, which is the examination of the heart tissue in the Klotz medium, and I have estimated from that that the concentration in the fresh heart was not less than 549 nanograms per gram. As you said this falls into both of the ranges. That is why by itself this would be inconclusive.

0. But coupling the two observations ---

If I can assume that the serum is a true specimen of serum then the finding of 491 in the specimen of serum is consistent with



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death due to digoxi	n.
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- Q. Can you take the next step then or the further step to say that in fact this child was the subject of toxic levels of digoxin? Can you say that with some degree of scientific certitude?
 - A. Would you repeat that, please.
- 0. Can you go one step further and can you tell this Commission whether or not with some degree of scientific certainty that this child was administered or was the subject of toxic levels of digoxin?
- Well, my function as a Α. forensic toxicologist is to assist the medical personnel, pathologists and so on, by telling them that a finding, a certain finding is consistent with death due to poisoning, meaning it could account for it.
- Well, I am not asking for 0. cause of death.
 - Α. All right.
- 0. I am asking for whether this child received from the material you have toxic levels of digoxin?
 - Α. Well, assuming it is a true



Cimbura, cr.ex. (Olah)

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specimen of serum I would expect certainly toxicity from that, yes.

Thank you.

Now a couple of other questions: in the case of Exhibit 95C, page 2, in particular Samples T60 at the bottom of page 2 and Sample T61. Those are samples of the Lombardo child, and there is presence of digoxin in the stomach and the contents of the small bowel.

I am sorry, I lost the number of that page.

I am sorry. You are having problems because of the dates. I am not giving you the dates.

This is the report of March 25th, 1982. Okay? And I am asking you to consider the very bottom analysis on page 2 and the very top on page 3.

A. Yes, I have it now, thank you.

All right. You will recall 0. that this relates to the Lombardo child who as we believe did not receive any therapeutic doses of digoxin.

I wanted to ascertain from you,





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and I don't know if you can help us - this may be in the field of a pharmacologist - is whether the presence of digoxin in the stomach and the small bowel is indicative of the mode in which the digoxin got there; whether it is secreted or whether it is an oral injection, and I don't know whether that is beyond your scope of expertise. If it is, please don't hesitate to tell me that.

Α. My answer in any case would be I don't know.

MR. OLAH: All right. Mr. Cimbura, thank you. Those are all the questions I have.

THE COMMISSIONER: I am just wondering, Miss Kitely and Miss Jackman, have you satisfied yourselves or dissatisfied yourselves, whatever?

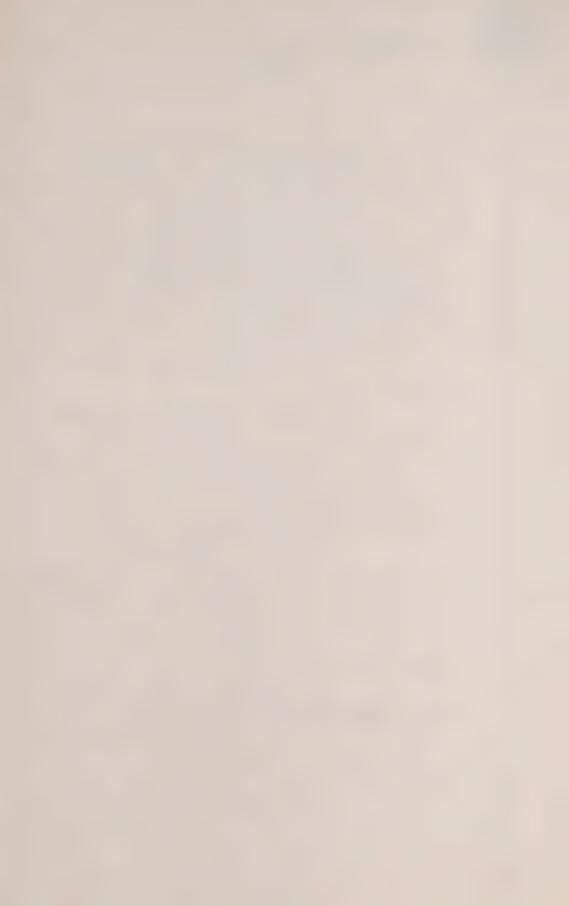
MS. KITELY: I think perhaps dissatisfied is the proper word for it. It appears that what I was trying to do cannot be done, but what I would like to do is put a couple of questions to reflect how the problem arose.

THE COMMISSIONER: Yes. All right.

When Mr. Lamek went through the

FURTHER CROSS-EXAMINATION BY MS. KITELY:

Mr. Cimbura, if you will keep Q. a copy of Exhibit 95 in front of you?



questions with you the other day you were careful
to point out by way of an example - let's look at
page 2, Item TllA, that where the words were used
A. That is page 2 of the
THE COMMISSIONER: Of the first
report.
THE WITNESS: Page 2 of the first

report, is it?

THE COMMISSIONER: January 11.

THE WITNESS: Sorry. Okay, thank you.

MS. KITELY: Q. Where the words are used, and I am quoting, "The tissue was found to contain 36 nanograms per gram calculated as digoxin of a mixture of digoxin and digoxinlike substances". That was from an RIA test? Right?



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A. What this terminology indicates is two methodologies were used here.

Q Right. What I have just read is IRA?

A. What you read is IRA and the --

 $\ensuremath{\mathfrak{Q}}.$ And the next sentence, and I

quote:

"The concentration of digoxin was 8 nanograms per gram ... ",

that is HPLC?

A. That is correct.

Q. Now, would you go to page 4 in the note; and let's look at Note 3 where the words are used:

"The concentration of digoxin ... ", you will agree with me that those words are consistent with what I have just read on page 2, which indicated on page 2 an HPLC result?

A. I have brackets after that (T42), is it Note 3 that you are wondering about?

Q. Yes.

A. It says:

"The concentration of digoxin in the heart muscle (T42) \dots ".

Q. Yes.

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A.	Would	you	look	up	my	identity	T42
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Q. Yes. T42 is a fresh specimen.

A. That is right.

Q. Can we do it my way for a second, Mr. Cimbura. Would you agree that the words that are used in Note 3, and I quote: "The concentration of digoxin ... ", are the same words that Mr. Lamek was careful to point out on page 2 were indicative of an HPLC test.

A. I am just getting a little bit tired, would you repeat that again, please?

THE COMMISSIONER: "The concentration of digoxin in the heart muscle ... ", did you refer to that, oh, " .. concentration of digoxin ... ", yes, all right.

MS. KITELY: I will approach it a different way, Mr. Commissioner.

THE COMMISSIONER: Well, approach it that way if I understood it.

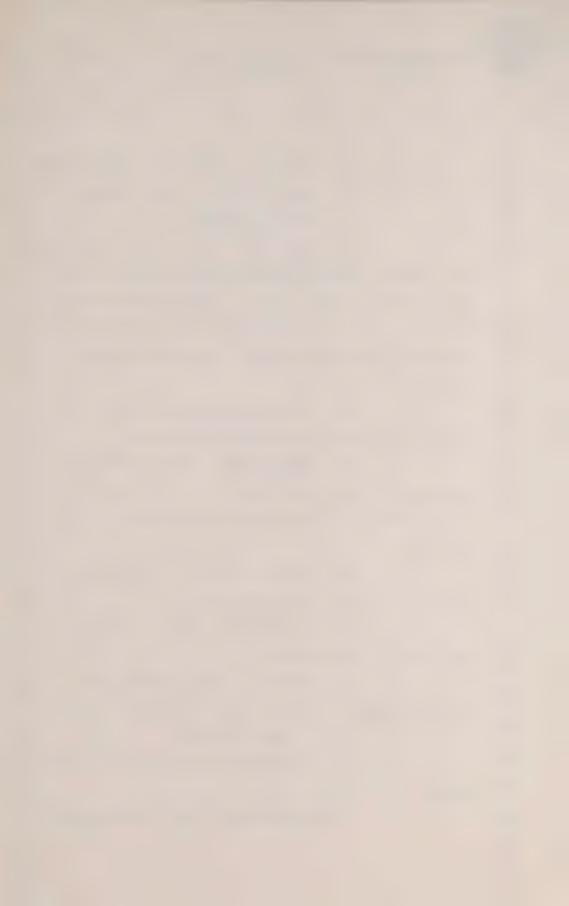
 $$\operatorname{MS.}$$ KITELY: Q. Am I correct, Mr. Cimbura, that we have no ranges for HPLC?

A. Ranges in what?

Q. Ranges for blood, heart, lung or

liver?

THE COMMISSIONER: Well, we have no



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ranges with figures that result from the HPLC, is that what you mean?

MS. KITELY: Yes.

THE COMMISSIONER: The ranges are the ranges of digoxin and ---

MS. KITELY: Q. Well, you have established that there are therapeutic ranges and fatal ranges, right, Mr. Cimbura?

A. In fresh autopsy specimens.

Q. Well, take it from there; we have no information before us as to therapeutic and fatal ranges where the sample was tested on HPLC?

A. On which specimens?

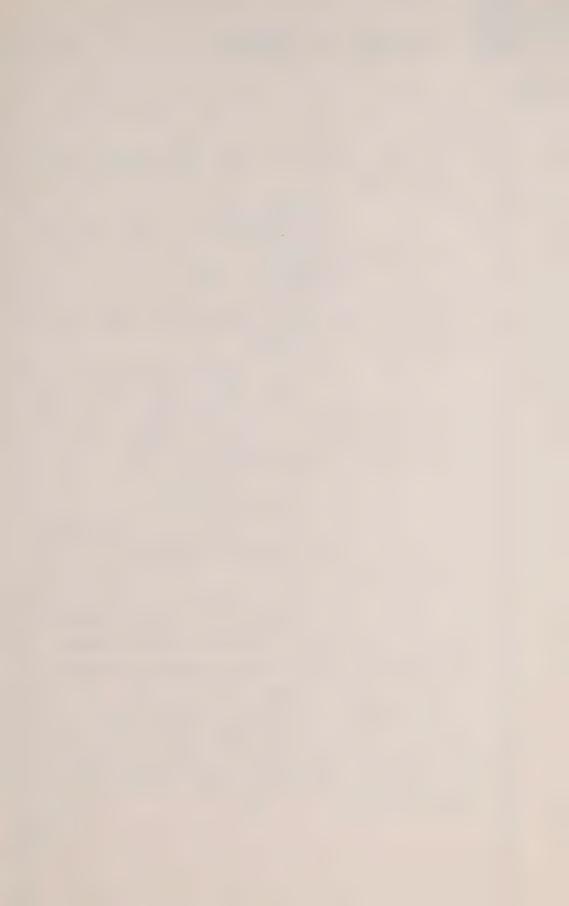
Q. Any specimens?

A. Well, for example if you combine my findings in these children you will have a range of HPLC values.

Q. But aside from using those, because you can't use those to establish the range because they are the children the Commission is interested in.

A. Okay.

Q. Aside from the children in Exhibit 95, there is no range of results using the HPLC; there is no therapeutic range, and there is no fatal range.



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That may be true, because it is A. based on literature and no one really at that time I don't believe used HPLC yet, they are beginning to use it now.

So wherever in your report you used the words I have referred to as an example on page 2:

"Concentration of digoxin was ... ", that being an HPLC reading, there is no range to stick that in, to compare it with?

In the controls that we studied in fixed specimens HPLC was not used, so there is no HPLC in the controls that we studied in fixed specimens, that's right.

And I understood you to say this morning when I was asking you about ranges, that you said the ranges on page 4 were at that time, and that in fact there are different ranges today?

Depending what tissue is involved A. there may have been - there were some additional reports which would change the range of course; and there were additional findings in my research which would change the range, that's right.

I think in our discussion at lunch time your concern was that if you had to find



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1983	rang	jes	it	would	require	you	to	do	an	exhaustive
study	of	the	: 1:	iteratı	ire?					

A. It would require that, yes.

MS. KITELY: Those are all the questions I have. Thank you. Might I say I would like to thank Mr. Hunt for making Mr. Cimbura available over the lunch hour.

THE COMMISSIONER: Yes. It is not all abuse, on occasion you get a kind word.

Miss Jackman, do you have any questions?

CROSS-EXAMINATION BY MS. JACKMAN:

Q. I want to clarify what, exactly what the levels mean in terms of the levels that you found, or if they mean anything. You have already said there was a problem with tissues, but there was blood and there is some certainty if it is post mortem.

A. I am sorry, I didn't quite hear you, would you repeat it, I am not hearing it?

Q. One of the things that I believe you were suggesting yesterday you would say you would be more certain of the level meaning something if it was a blood post mortem than if it was a tissue post mortem?

- A. Yes, that is correct.
- Q. Or the significance of it?



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A. Yes.

Q. In terms of Exhibit 95 you have put the levels within ranges, toxic and fatal ranges, some of them?

A. I tried to put it whenever I could, that's right.

Q. Now what I would like to know,
Mr. Cimbura, is how much information you had about
the child? Exhibit 212 seems to indicate that you
got a one-page note from the Hospital on the different
samples, were you given the children's charts?

A. Are you referring to the control children?

Q. No, not the control children, I am talking about the children that are the subject of this hearing?

A. The children under investigation?

Q. Yes.

A. At some stage or other, yes. For example I have now a detailed summary of all clinical history and all clinical findings and so on. I am not sure, it was probably at a later stage.

Q. After you had done the tests?

A. Pardon me?

Q. After you had done the tests?



(2)

A. After I had done at least some tests, yes. You see, our tests were continued as you know until when - until, the last report was December last year, so I am not exactly sure when I received all the information that I have now. But at the beginning I would not have received that, I would receive from the police usually much less information, less then I usually want.

Q. The information that you did get, the detailed summaries of the children, the children's condition, would that have been in 1982 that you were given that, or in 1983, can you estimate around when?

Perhaps I can put it this way. Did you receive it do you believe before you did your first report for Sergeant Warr and Dr. Tepperman on January the 11th, or for Mr. McGee, I should say.

had a complete history yet then but I had quite a lot of history. You know, because we talked about, there were many meetings and discussions and many of those aspects were being continuously discussed.

Q. So what kinds of information would you have from them in terms of doing the testing around the child's history?



 yes.

	A.		I	may	have	ha	ad an	ny kind	i o i	E	
information	that	was	a	vaila	able	at	one	stage	or	another	

Q. What I am trying to get at, were you told if the child had renal failure?

A. Well, that was a question I specifically asked myself you know, yes.

Q. Were you told if the child had a congestive heart, congenital heart disease or congenital heart failure?

A. I may have known that information,

Q. You think you may have but you are not certain when?

A. That is right.

Q. Mr. Cimbura, when you are looking at the levels that you have come, arrived at through the testing, would it be safe to say that each level, the significance of each level depends on the child itself, the child's condition?

A. I don't think I can answer that, what sort of significance are you talking about?

Q. Well, for instance, if you had a child with high blood level, a high digoxin level in the blood post mortem, and you were to find out subsequently that that child had had severe renal



failure, then that level would mean something different to you in light of the fact the child had renal failure than if the child didn't have renal failure?

A. Yes, basically.

Q. So that with these levels when you are putting them within the ranges they may not actually - if some level for instance is within the fatal range because of perhaps renal failure or something like that, it could in fact not mean that it was consistent with a fatal dose such that it might be the cause of death?

A. Well, it would - for example if there was a renal problem of course it would be a problem to determine to what degree that could attribute the totality of the findings. So a level that falls into the, that falls clearly into the fatal range for blood is consistent with or could account for death, could, I mean that is a possibility, other factors to be investigated.

Q. And if the other factors were investigated it could account for it, but the other factors could take it out of that fatal?

A. It may or may not depending on many things, yes.

Q. Depending on the factors?



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A. Depending on the extent of renal failure and the degree of the level and many other considerations, yes.

Q. Now, when you were suggesting the ranges in Exhibit 95 in your report, and you were stating the particular findings as being within a therapeutic or a fatal range, you were not adjusting that in light of the child's clinical condition, were you, when you did that?

A. No, I don't believe so, no.

Q. Would it also be fair to say that contamination could in fact also affect the significance of a finding?

A. If you could prove it, certainly.

Q. So that a finding that could be in a fatal range, if you could show that it was contaminated may not mean anything at all?

A. Obviously contamination is something abnormal.

Q. Mr. Cimbura, these findings and the statements that they are within a therapeutic or fatal range do not reflect any adjustment for contamination or anything like that as well, is that correct to say?

A. They do not reflect any adjustment for contamination?



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you	assumed	l they	wei	ce no	ot.		

If I knew a sample was contami-A. nated I would not have included - I would have mentioned that in regard to my finding.

If you didn't know the sample was contaminated or not would you check it out, find out if it was, or would you just assume it wasn't?

It is not easy, there is no way I could check it.

So you would assume it was not 0. contaminated unless you were told that it was?

Unless there was some proof that it was, that is right; some proof or some suggestion, or some theory; or some history; or something.

0. Now the research studies, the control studies that you have done in Exhibit 213, when did you begin doing those studies, approximately?

> Yes, which is that again, I am A.

> > 0. Exhibit 213.

were started and when they were finished?

Are you referring to this bundle? A.

Yes, I want to know when these

Well, some of them were started





ANGUS, STONEHOUSE & CO. LTD. Cimbura, cr.ex. (Jackman)

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as early as April/May 1981, or around that time anyway.

> And when did you complete Q.

them?



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Q. The samples that you used for the studies, were they all provided to you from the Hospital for Sick Children?

A. Yes.

 Ω . So, these are infants who died at the Hospital?

A. That's right.

 Ω . That's right.

A. I am making a general ---

THE COMMISSIONER: You are guessing

that that is so?

THE WITNESS: Pardon me?

THE COMMISSIONER: You are guessing

that, are you?

THE WITNESS: Yes, I will have to

examine it.

THE COMMISSIONER: I think we have

heard evidence that ---

THE WITNESS: I believe my

recollection is that, sir ---

THE COMMISSIONER: --- a great many autopsies takes place at the Hospital for Sick Children for children who died elsewhere?



THE WITNESS: As far as I can recall it, at least the majority of them came from the Hospital for Sick Children, and perhaps all, yes.

MS. JACKMAN: Q. Now, Mr. Cimbura, I note in some of the studies that you have done there is a notation, for example, on page 17 of Exhibit 213.

A. Yes.

Q. Note No. 3 is the deaths were due to causes other than digoxin poisoning. How were you aware of that?

A. Well, I would be aware of any death there by my function, that was due to the digoxin poisoning.

 Ω . No, but would the Hospital tell you that the children, that their cause of death had been decided to be something other than digoxin?

A. I would be told by the chief coroner if there was such a thing and I have discussed with the chief coroner for the Province.

Q. And would that be true as well with the children that you studied that are the subject of this investigation?

THE COMMISSIONER: Would what be true?



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MS. JACKMAN: That he was aware that there were other causes of death aside from digoxin poisoning.

THE COMMISSIONER: If he knows the answer to that perhaps we can close the shop and go home.

MS. JACKMAN: No, Mr. Commissioner, I'm not saying that that was the cause of death, but a number of the children, their final autopsy reports, or the discharge summaries give different causes of death other than digoxin poisoning.

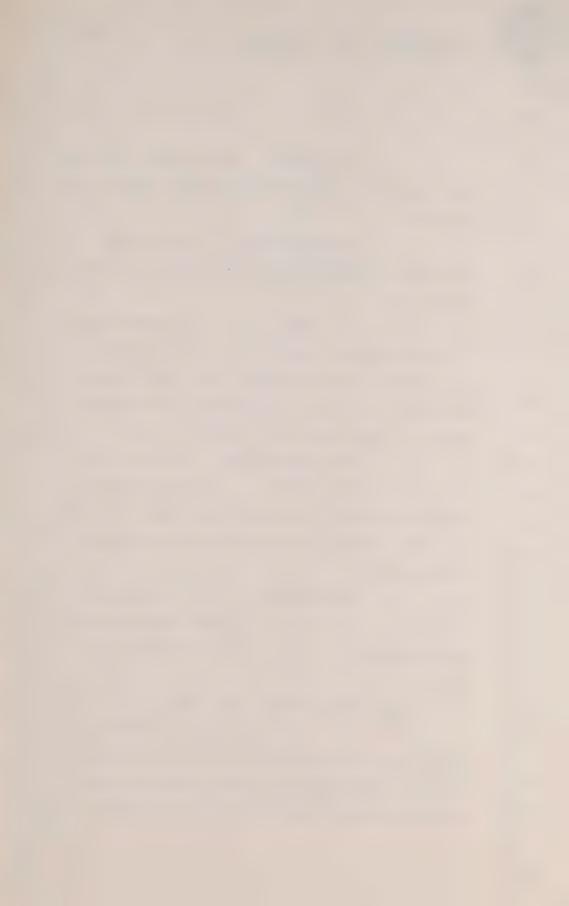
THE COMMISSIONER: Oh, yes, I see.

MS. JACKMAN: I am just asking him if he was aware of those different causes of death for these children that are the subject of this investigation.

THE WITNESS: As I have examined the medical charts of all of these children as part of my research, so, I was aware of these things, yes.

MS. JACKMAN: Ω . Okay.

A. If I may qualify myself,
medical charts of many of these children. On some
of them I didn't need to go to the medical charts
because information was provided to me by the



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Q. Now, on Exhibit 213 on Graph 11 - or page 11, sorry, this was a control study, I understand. Is it possible that the same up and down curve could occur in the tissues of a child who has died?

A. By up and down you mean the little blip there further down?

 Ω . Where it goes up at 50 days, between 40 and 50 days.

A. There is that possibility,
I couldn't rule it out, that's right.

 Ω . It is a possibility. Is it also possible at least theoretically that it could be over a shorter period of time, or you wouldn't know?

A. That I can't answer because I don't know. In this study the increase is around 40 to 45 days.

O. Yes.

A. 'And I haven't seen it anywhere

 Ω . But you couldn't exclude it not knowing if in fact it could be a shorter period of time?





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Well, I could exclude it if an experiment was carried out under identical conditions as this was carried out.

0. But an experiment like that wasn't carried out.

- Well, it was. Α.
- 0. No, I mean in the child?
- Α. Oh, in a child.
- Ω . I'm talking about in the tissues of a child.

No, you would have to analyze Α. the samples over many days.

Q. Now, going back to Exhibit 95 on page 2, sample T27.

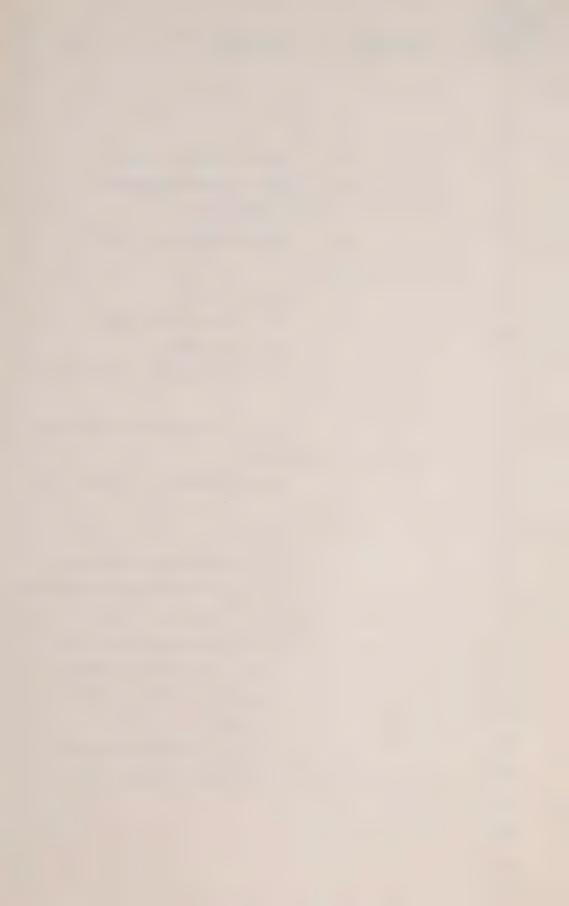
> Yes. Α.

0. For Justin Cook is shown to be J05490 and you found that it contained 46 nanograms per millilitre of digoxin. Now, if you look at Justin Cook's chart, which is Exhibit 116 on page 57.

- I don't have that to look at. A.
- I can just show you mine. 0.
- A. Oh, okay.
- On page 57 there is the same number J05490, which is the second column from the outside.

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- J05490? A.
- Q. Yes.
- Α. That's right.
- Q. And it shows a level to be

68 nanograms?

- That's right. A.
- 0. Mr. Cimbura, can you account for the discrepancy in this case because it would seem there is a 22 nanogram difference and if you compare that with the 46 nanograms that were found in your testing that would be almost 50 per cent discrepancy between the two samples.
 - Α. 68 to 46?
 - 0. Yes.
- A. I don't have my calculator here. I think 50 per cent - if it was 50 per cent it would be ...
- I was putting the 22 on the Ω. 46 not on the 68.
 - Α. Yes.
- 0. Between one-third anyways, almost, one-third to a half discrepancy depending on which figure you are using. Have you any idea why that discrepancy should be there. Perhaps I should put it to you, does it surprise you that the



discrepancy is that large?

A. Well, this is a little bit higher. Assuming it is the same sample, which the number J, I don't know what it means, this is just one of the labelling and I don't know, you know, how valid one can compare them.

 $\Omega.$ Well, assuming that it is the same sample because it is the same number.

A. Assuming it is the same sample the only conclusion I can reach is that our results is lower and part of the, some of the reasons that may account for it is the reasons I have explained before that we extract and we lose some. We use a different antibody and that's part of the reasons for that.

Q. Now, I believe there is also another discrepancy like that on page 5 of Exhibit 95A, which is T29 on the bottom of page 5, you found a level of 69 and in the chart for Allana Miller, which is Exhibit 115, the same appears.

THE COMMISSIONER: What page is that?

MS. JACKMAN: Oh, page 70, Exhibit

115.

THE COMMISSIONER: Yes, all right.

THE WITNESS: Yes. I notice in my



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report I have a question mark after the number meaning that I couldn't read it very well, but it appears to be the same, that's right.

THE COMMISSIONER: I'm sorry, you are comparing this with what page?

MS. JACKMAN: Exhibit 115, page 70.

THE COMMISSIONER: What's the

figure there?

by Mr. Cimbura's team.

MS. JACKMAN: Is 78.

THE COMMISSIONER: 78 and 69?

MS. JACKMAN: And 69 was the finding

Q. Mr. Cimbura, in light of those kinds of discrepancies, does that make more questionable the accuracy of the findings either for the Hospital or for the Centre?

A. Well, the last two findings are very comparable.

THE COMMISSIONER: I'm sorry, I'm

MS. JACKMAN: The 69 and the 78.

THE COMMISSIONER: I'm sorry, the

specimen number, have you got that?

MS. JACKMAN: It is at the bottom of

page 5, Mr. Commissioner.



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THE COMMISSIONER: I	saw it but the
number doesn't seem to be the same.	Oh, you are
uite right, I'm sorry, yes, you are	quite right.

MS. JACKMAN: Ω . Are there anything such as ranges in terms of how far you can go in having different readings on the same sample?

- A. Well, obviously that would depend on the type of the sample, the level, the condition of the tissue, many factors.
- Q. But if I am reading for instance the 69, should I be saying, well, that should be 69 minus 12 or plus 12, it could be either if I'm going to be accurate about it?
- A. Well, I would think that the difference between two laboratories, between what was it that they got?
 - Ω . 78 and 69.
- A. 78 and 69 would be quite comparable; certainly comparable within toxicological intent.
- Q. Okay. I just had one further question and it is from something you said the last time you were here. You had stated that there was a possibility that your recovery studies might be published and you have given us the recovery studies



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that	you	did. I	Have t	hey k	been	publ:	ished	yet	?	
		A	•	No.	I am	plai	nning	to,	they	
have	beer	accept	ted fo	r pres	senta	tion	at th	ne Ai	merican	
Acade	emy c	of Fore	nsic S	cience	es wh	ich i	is ne	kt F	ebruary	

Q. Next February. Thank you.

THE COMMISSIONER: Thank you.

Mr. Labow?

CROSS-EXAMINATION BY MR. LABOW:

Q. Mr. Cimbura, with reference to Exhibit 95C, that is your report of March 25th, Sample No. T46.

- A. What page on that report, sir?
- Ω . First page.
- A. Yes.
- Ω . Sample No. T46.
- A. Yes, sir.
- Ω. Was it ever indicated to you

that that sample was contaminated in any way?

A. Well, as I indicated, what was indicated to me was that it was heated for a certain time under a certain temperature.

Q. And my understanding is that you told Mr. Lamek that you then simulated an experiment with serum and heated it and found that there was no significant change in the digoxin

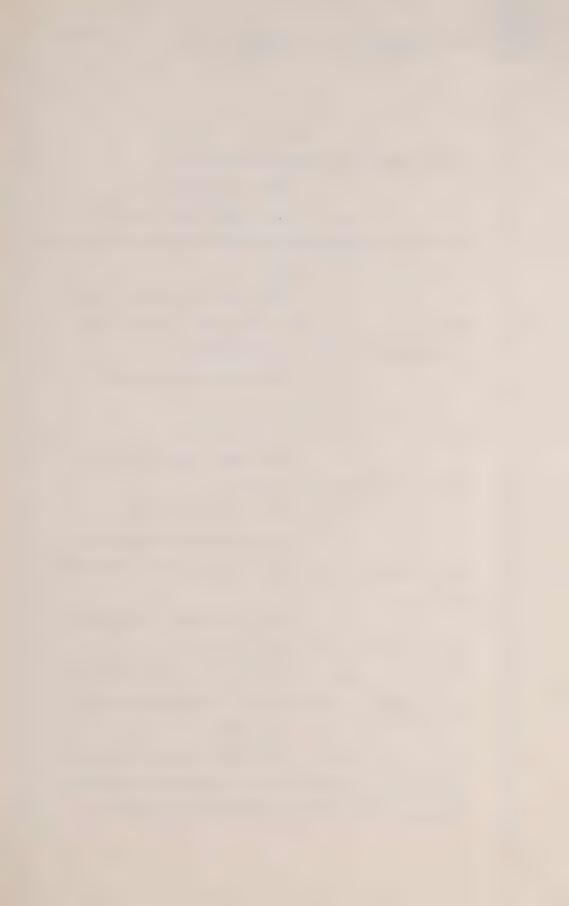
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2	reading before or after the heating?							
3	A. That is correct, sir.							
4	Q. Now, other than that, was							
5	there any indication to you that this was contaminated?							
6	A. No.							
7	Ω. Now, I'd like you to look at							
8	Exhibit 213. It is the sixth page entitled "RIA							
	Intraassay Precision Heart Tissue".							
9	A. Which page again, sir?							
10	Ω. 6.							
11	A. 6. Yes, sir.							
12	Ω. Now, there were only two							
13	children studied in this test.							
14	A. That is correct, sir.							
15	Q. Do you know when the second							
16	child, that is No. 3, received his or her last dose							
	of digoxin?							
17	A. I may have that information							
18	but I don't have it with me, sir.							
19	Q. If you could find it and tell							
20	your counsel I would be very interested to know.							
21	A. All right.							
22;	Q. Now, before your results are							
23	looked at by someone trying to determine the cause							
	of death, do we have to know in many of the							



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instance	s whe	n the	last	dose	of	digoxin	was	receive
for thes	e chi	ldren	?					

A. Are you referring to these control experiments?

 Ω . Yes.

A. Yes, and it is indicated on other documents from them.

 Ω . Right.

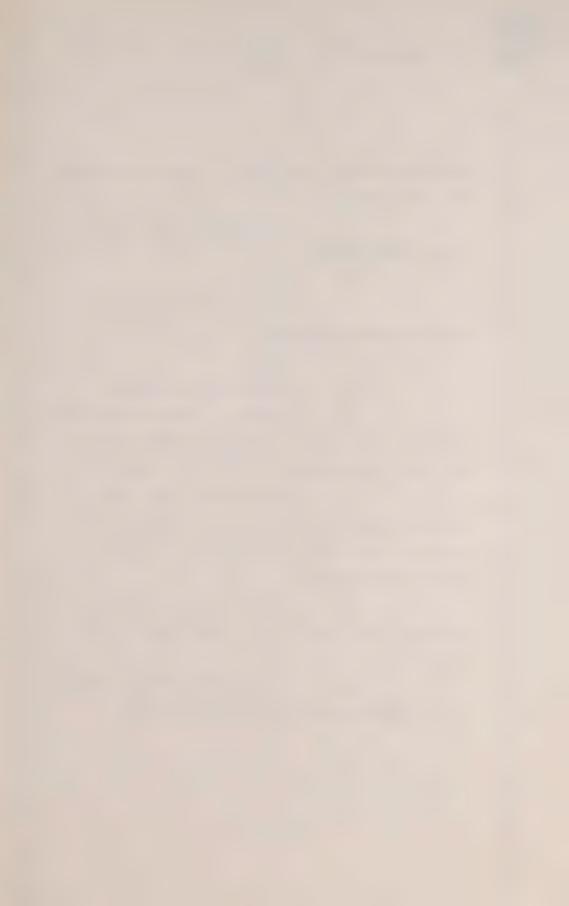
A. You have that available.

Q. In some of the other documents it indicates that there was the interval between last dose and death was a certain time period?

A. That's right, yes. The reason it wasn't included here was because for the purpose of the study the interval was not for the specific purpose.

 $\ensuremath{\text{Q}}.$ You were only trying to find the lower range and the upper range in that study? '

A. That was one concern, and to find the intraassay variation, that's right.



questions.

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MR. LABOW: I don't have any other

THE COMMISSIONER: All right.

Mr. Tobias?

CROSS-EXAMINATION BY MR. TOBIAS:

 Ω . Yes, Mr. Cimbura, my name is Warren Tobias. I act for the family of Jordan Hines.

I believe you told my friend Mr. Olah that with respect to children who were not on digoxin therapy at all and had not been administered digoxin you would have expected in doing your assays to find no digoxin at all.

Is that correct? Did I understand the response you gave?

A. That is right.

 Ω . Now, I would like to ask the same question but in a much more specific set of assumptions.

I would like you to assume that you were given a sample of heart tissue that was taken at autopsy and preserved for a three-month period in Klotz fixative solution.

The other fact that I would like you to assume is that given that sample, you were

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also given the information that that child had not at any time during life had digoxin in any manner whatsoever introduced into its system and that you were to take that as the given fact. That was something that you knew.

THE COMMISSIONER: Mr. Tobias, you mean he had not had it prescribed?

MR. TOBIAS: No, I'm going further

THE COMMISSIONER: All right.

MR. TOBIAS: He is to take as a fact that no digoxin had been introduced into the child's system during life.

THE COMMISSIONER: All right.

MR. TOBIAS: Q. Now, in doing your RIA, HPLC assays on that particular sample, would you also agree that you would expect in those set of circumstances to find no digoxin?

A. If that was from a child who was not supposed to be administered --

 Ω . Yes.

A. The only difference is the heart is placed into Klotz medium?

Q. That is right.

A. And stored there for two



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to three months?

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Q.

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That is right.

Α. That is right, I would

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expect to find no digoxin.

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0. Now if in that same set of circumstances you did find digoxin on the assay and the level I am going to suggest to you is a level of, let's say, 250 nanograms, would you then draw the conclusion that at some time digoxin had been introduced into that child's system?

Assuming that was not placed into that Klotz solution after death.

> 0. All right.

Let me give you the other assumption.

Assume that it was placed into Klotz solution.

It was not placed?

 Ω . No, no, I am asking you

to assume that it was placed in Klotz solution.

THE COMMISSIONER: Are you talking about the heart, digoxin in the heart tissue?

MR. TOBIAS: I am saying the heart

tissue.

THE COMMISSIONER: Are you talking about heart tissue or are you talking about digoxin? MR. TOBIAS: Oh, I see your point,



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Mr. Commissioner.

Assuming that no digoxin had been put into the Klotz solution after death, and assuming that no digoxin had been introduced into the child's system during life, and assuming that you had the same sample that had been preserved in Klotz fixative three months, and you did find diogxin under assays, would it then be your conclusion that somehow digoxin had been introduced into that child's system before death?

A. May I repeat --

Q. Yes.

A. -- just to see what I think

is correct?

O. Yes.

A. If I find digoxin in a

heart, fresh heart specimen, that has been stored in Klotz fixative for a period of three months; is that it?

 Ω . Yes.

A. And if I can assume that no one put that digoxin into the Klotz solution --

Q. Yes.

A. -- in the period between death and analyses; is that right?

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Ω.	Ye	S	9
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A. Then the child -- I believe that the child received digoxin before death, that is right.

Ω. All right. Thank you.

Now with respect specifically to your result interpretation on Jordan Hines, I believe in your report you said that it was your conclusion that the fresh heart tissue would have had no less than 250 nanograms per gram of digoxin before it was fixed into Klotz solution?

That was your conclusion, was it not, doctor - or Mr. Cimbura, wasn't it?

A. I believe it was. Maybe I should look it up. What page was it, sir?

Q. I believe it was page 6 of Exhibit 95A. That was your January report. Or if not on page 6 then on page 7.

A. Yes, on page 7, that is right. I have it now, yes.

Q. Before you drew that conclusion, as I understand it, the specimen that you had consisted of heart tissue of Jordan Hines which had been taken at autopsy from the right atrium, the left ventricle and the septum; is that correct?



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			Α.	The	e hea	art or	gan wa	s, as
Ι	understand	it,	placed	into	the	Klotz	after	the
aı	utopsy.							

 Ω . Yes.

A. And when I received it I arranged to dissect it into the regions.

 Ω_{\bullet} I see. So that what you are saying is that at autopsy itself the heart was placed in Klotz solution?

A. Yes.

Q. Then you arranged to have it dissected and you took samples from the left ventricle, the right atrium and the septum; is that correct?

A. Essentially, other than saying I am not sure whether it was completely intact, fairly intact. There may have been a small piece taken out of that heart for other studies at the Hospital at the time.

Q. I understand. But in any event the tissue samples that you ran the assays on were from the left ventricle, the right atrium and the septum. Do I have that correct?

A. That is right, sir.

Q. All right.



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Now do I take it with respect to the right atrium you did not do both RIA and HPLC?

- A. That is correct.
- Q. But with respect to the left ventricle and the septum, on those samples you did both the RIA and the HPLC techinques; is that not correct?
 - A. That is correct, sir.
- Q. All right. And that is why you were able to come to the conclusion that with respect to the left ventricle the concentration of digoxin was 52 and with respect to the septum the concentration was 89?
 - A. That is correct, sir.
 - Ω . All right. Fine.

Now with respect to results on the heart of Jordan Hines, and those are the assays that you have just talked about, those that were not on exhumed tissues, am I correct?

- A. No, this was tissue, as I understand it, placed in the Klotz medium, Klotz solution.
- Ω. Okay. Now I understand there were further assays done later on liver tissue that was from exhumation; is that correct?



Q. All right. Specimen T44

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EE8 2 Α. I believe so. Can I find it out in my report? 3 Please look at Exhibit 95C, Q. 4 Mr. Cimbura. 5 It is the report from Α. 6 February 2nd, is that right, I believe? No, I'm 7 sorry, I still don't have it. I will find it. 8 MR. OLAH: It is 'T44 in Exhibit 95A, 9 Mr. Commissioner. MR. ROLAND: And it is repeated in 10 95B. 11 THE COMMISSIONER: __T44? 12 MR. OLAH: Yes, sir. You will see 13 it is labelled liver, reported to be from autopsy 14 after exhumation. 15 THE COMMISSIONER: All right. MR. TOBIAS: Yes. That is 16 correct. 17 That report, Mr. Cimbura, Q. 18 dated February 2, 1982. 19 A. Well, the first part of that 20 finding is on the first report that we discussed. I 21 think I will have to go back to the original report 22 we discussed with respect to Baby Hines.



Cimbura cr.ex. (Tobias)

EE9

on page 7 of the first report --

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A. That is correct.

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Q. Now assays were run on

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liver tissues which were from exhumation.

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A. Which were...?

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O. Which were taken after the

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body was exhumed.

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A. That is correct, sir.

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 Ω . I understand you already

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indicated yesterday to Mr. Lamek that you have some

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concern with respect to interpreting your readings

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when you are dealing with tissue which was fixed in

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Klotz solution.

I also understood that you indicated

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to Mr. Lamek that you have still more concern with

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respect to interpreting readings that you found when

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it comes to exhumed tissue.

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So I am not going to ask you to interpret it for me. I am only going to ask you this:

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On the basis of the assays that you ran on the liver

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tissue that was taken after the body was exhumed, are

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you reasonably confident with some degree of scientific

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certainty that what you found was digoxin without commenting at all about the levels or what they mean?

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A. Yes.

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states.

Q. Okay. You are:

A. Yes.

Q. And your conclusion would be that it was digoxin that you found on those tissues. Correct?

A. That is what my report

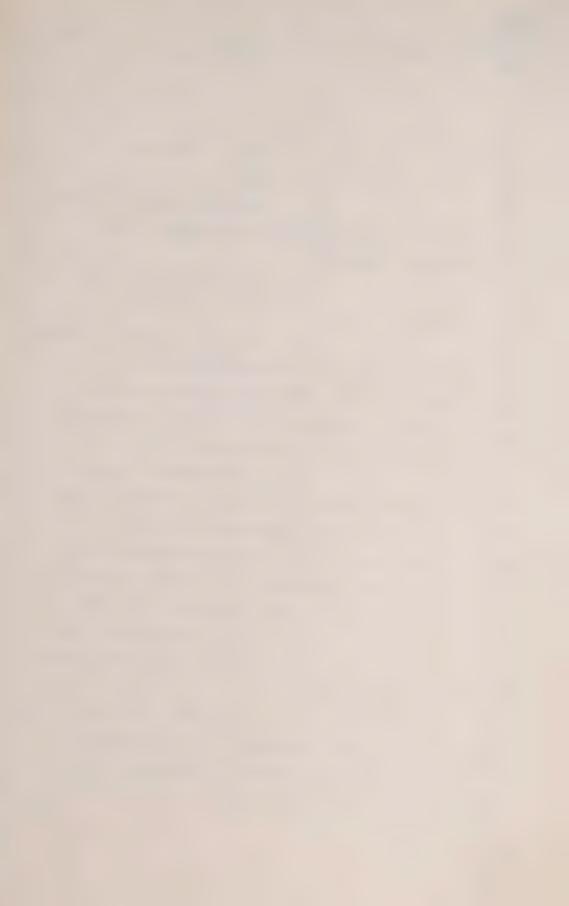
Q. All right. Now this morning you were asked by Mr. Roland whether or not with respect to Jordan Hines you subjected the Klotz fixative to the high pressure liquid chromatography method, and I believe that you said no.

When you were asked by him how you could be sure or you could be confident in your estimate of the 250 nanograms in the heart tissue, you indicated that one of the assumptions that you made was that any digoxinlike substance in the Klotz solution would have been derivatives of digoxin.

That was your answer was it not?

A. That was my stated assumption, that is right.

Q. All right. Now I would like to see if I can understand that because that is rather important to me that I understand why you were able to give that answer.



EE11

When you first appeared before the Commission on June 22, 1983, I recall discussion between Mr. Lamek and yourself whereby you told Mr. Lamek that there were basically two groups of things which could cross-react with your digoxin antibody. Do you remember that discussion?

MR. HUNT: I'm sure he doesn't remember. Have you got the page?

MR. TOBIAS: Q. All right. If I can be of some assistance, Mr. Cimbura, I am referring to Volume No. 2, page 112. I won't read it to you word for word, but tell me if this jives with your recollection of your evidence.

I believe that one of the things that you told Mr. Lamek is that one of the groups that would tend to react with your digoxin antibody was the metabolites of digoxin; is that correct?

A. Yes, that is true, yes.

Q. Okay. And I think you also told him that the other group of things that you would expct to react with the digoxin or cross-react with the digoxin antibody were chemically -- chemicals which were molecularly similar to digoxin.

Is that also correct?

A. I don't recall exactly --



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MR. LAMEK: At the foot of page

112.

THE WITNESS: I may have been referring to digoxin derivatives such as --

MR. TOBAIS: Q. Well, in particular I am referring to Lanatoside C which was one example you gave of a drug which was molecularly similar.

A. If you are referring to that, yes, that is very similar to digoxin, yes.

 Ω . Okay. Fine.

Now first of all with respect to the metabolites, is it true that basically what they are is a derivative of digoxin in this sense: in the sense that after digoxin is administered and after the body works on the digoxin it breaks it down into its derivative components. Is that a fair statement?

A. With respect to metabolites, those are products of digoxin produced by the body, that is right.

Q. All right. What you told us at page 113 the last time you were here is, and Mr. Commissioner, to assist you, this is three lines from the bottom of page 113:

"Of course, as I mentioned previously, the metabolites or the breakdown products of digoxin are



produces?

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produced in the body after digoxin is administered."

Do you recall giving that evidence?

I put to you again have I under
stood you to mean by that that basically the metabolites of digoxin are derivative products which the
body in acting on the digoxin after administration

A. I suppose you could call it that. It is a technical definition of what derivative means...

Q. All right. It is a fairly ineloquent summary, but I have got the principle right?

A. I think in a sense I think

what you are saying is correct.

Q. All right. So do you agree with me in order to find the metabolites one would first have to inject or introduce into the body the digoxin? If there were no digoxin there would be no metabolites of digoxin in the sample?

Do you agree with that?

A. That is what I would understand, that is right.

Q. Now with respect to the other factor, and that is the chemicals or the drugs



EE14

something?

that are molecularly similar to digoxin, I take it that when we are talking about Klotz solution you know what the chemical makeup of Klotz solution is?

A. I know the composition,

that is right.

Q. So that you would know whether any of these similar chemicals were in Klotz

solution and obviously you are satisfied that they are not?

A. Well, yes, I see -- I'm sorry, I see what you are getting at.

Part of the documents that I have introduced is that Klotz solution does not react with the RIA, that is right.

 Ω_{\bullet} Exactly. So there would be no reason because of that to subject it to the HPLC in order to separate digoxin from digoxinlike substances.

Is that correct or have I missed



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		Α.	7	Well	Ι	know	that	the	Klotz
solution	does	not	react	with	1 1	the F	RIA.		

- And if you did find anything that cross-reacted those would be the metabolites, is that correct?
- Α. And the substances that are in the Klotz solution, the derivatives of the substances which I believe are derivatives of digoxin.
 - 0. Exactly.
- A. I have not been able to identify them, I don't know what they are.
- 0. My point is this, Mr. Cimbura. If you tested the Klotz solution and you found a positive reading you would know it was either digoxin or the derivatives of digoxin that was reacting with the antibody?
- A. Well from that point of view if that was the only specimen I had ---
 - Q. Yes.
- ... I would want to do HPLC. You know, in these cases HPLC was done on some regions of the heart.
 - Yes. Q.
- To let me know there was digoxin present.



′)

			Q.		No,	no,	Ιá	am re	eferri	ng now	
only	to	the	assay	that	you	run	on	the	Klotz	solutio	r
itsel	f.										

A. That is right. So I have not run HPLC so that it could be.

Q. I am sorry, it could be?

A. If I haven't run HPLC I wouldn't be able to express any digoxin in that Klotz medium.

Q. Digoxin as opposed to the digoxin metabolites; what I am saying is if you ran the assay on the Klotz solution itself and it produced a positive reading, you would know that what you were reading was either digoxin or digoxin metabolites, is that fair?

A. Well, I believe I would have to know also that in some part of the specimen there is digoxin as identified by HPLC analysis, which happened in the specimen of Cook.

Q. Right.

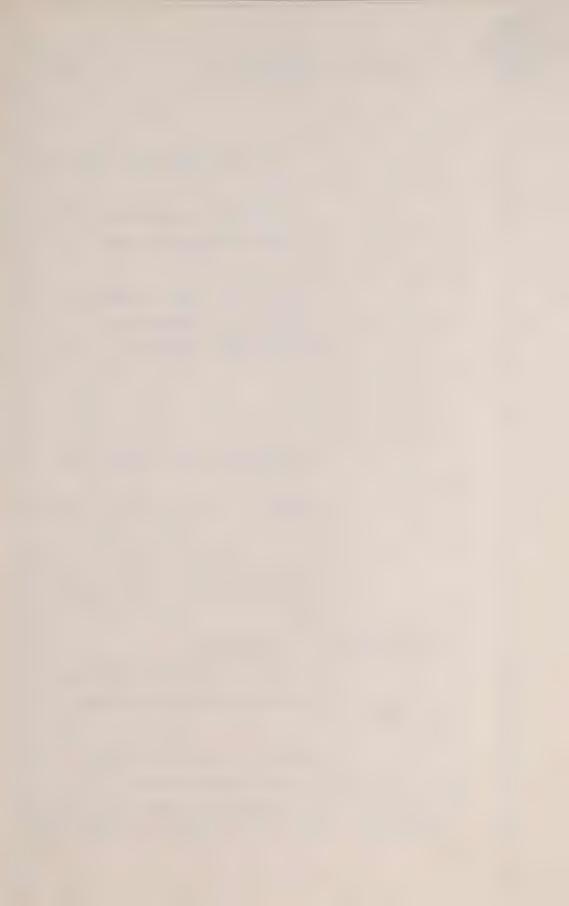
A. I'm sorry, I mean the specimen of Baby Hines. As you noticed, as you said yourself the left ventricle was analysed by both HPLC and RIA?

Q. Yes.





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	2	A. And the digoxin was identified.
	3	Q. Yes.
	3	A. So that in combination with
	4 1	that finding I could make the conclusion that you
	5	wanted to have.
	6	MR. TOBIAS: All right. Thank you,
	7 (those are all my questions, Mr. Commissioner.
3	8	THE COMMISSIONER: Thank you, we will
	9 :	take 15 minutes.
		Short recess.
	10	On resuming.
	11	THE COMMISSIONER: Mr. Shanahan, are
	12	you next?
	13	MR. SHANAHAN: I am not, but I don't
	14:	mind.
	15	THE COMMISSIONER: Are you not next?
	16	MR. SHANAHAN: I don't think I am
		really, but I am ready.
	17	CROSS-EXAMINATION BY MR. SHANAHAN:
	18	Q. Doctor, my name is Shanahan
	10 (and I act for the families of Lombardo and Dawson
	20	children.
	21	Mr. Cimbura, if you could turn to
	22	the reports, they are all stapled together, but I
	23	think the ones for, the report for Amber Dawson are
		found at page 11 of your first report of January 11,
	24.	



1982.

	Now, as I look at it here	I think
you have made	it clear to Mr. Lamek that	the testin
that was done	there was both the RIA and	then the
RIA after the	HPLC, is that right?	

A. Which particular region of the heart are you referring to, sir?

Q. I thought you indicated that both the heart and the lung and the fluid, all of those testings had been done in duplicate in that manner and that you reached the conclusions that you have stated there. That is where I want to start from, is that right?

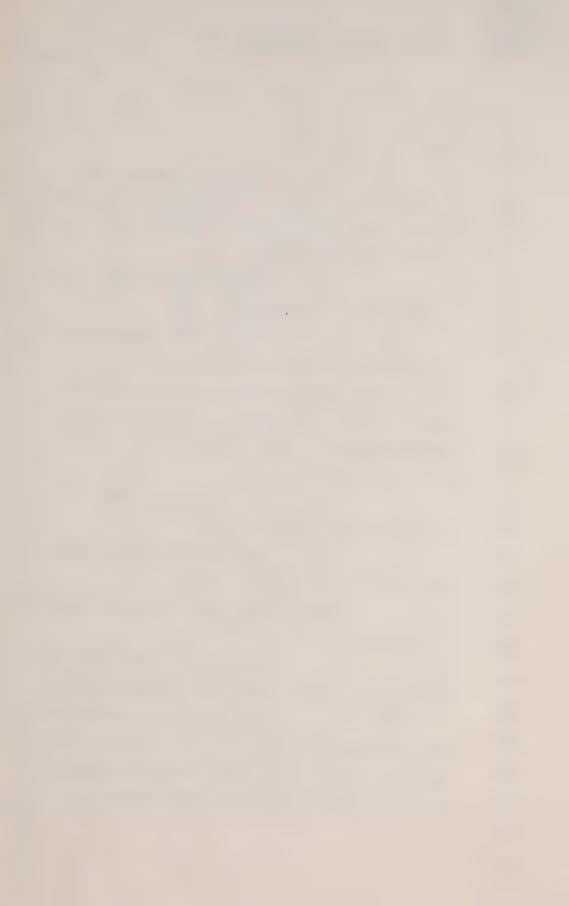
A. The conclusion, which conclusion, I am not quite clear.

Q. Well on the heart you have got "Left ventricle, septum, lung".

And you have got: "No digoxin could be detected".

A. That's right. That indicates that HPLC was done on those three, that's right.

Q. As I take it too, we know, we have heard sir, that the coroner was notified with respect to Amber Dawson, that the autopsy was done by Dr. Cutz at the Hospital for Sick Children. I



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take it that you did your sampling on all tissues that were provided for you, and it seems to me here quite obvious that you were never supplied with any autopsy blood with respect to Amber Dawson?

That is right, that is correct as far as I am aware, that's right.

Do you know, sir, and it is 0. a bit much to ask; do you know, was that ever discussed or requested, or did you ever speak to Sergeant Warr about that, as to whether there might be blood given that she was a coroner's case and that the autopsy had been done at Sick Children's Hospital; did that issue of her blood and the availability of it ever come up?

I feel confident it has, that is the information I was relating to the police that blood is a very useful specimen for analysis in all these children.

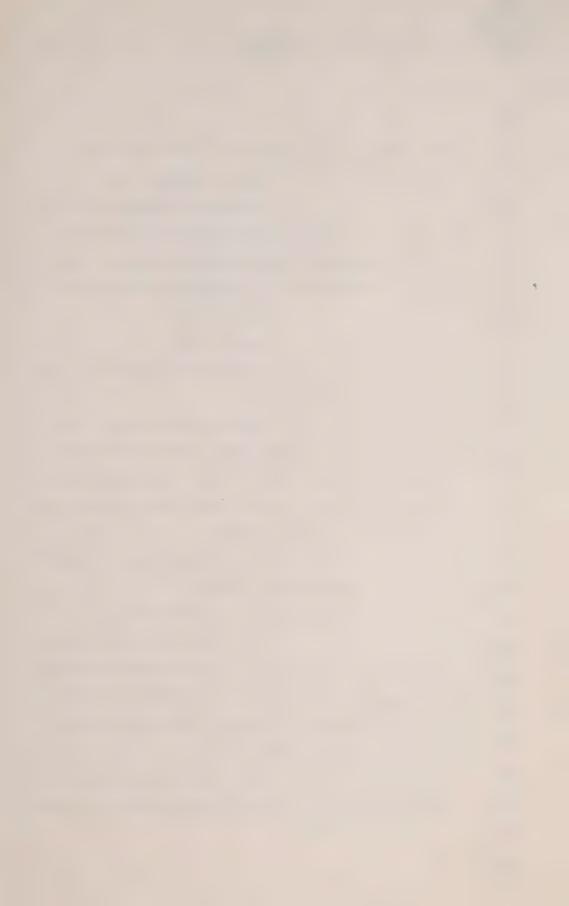
- Q. It would seem then that they probably looked for it and it just simply wasn't there?
 - Well, you can ask them. Α.
- Now, bearing in mind here as 0. well that you would have got here what seems to me to be tissue from the heart and lung of Amber Dawson



TORONTO, ONTARIO

that would have been fixed in a Klotz solution?

- A. That is correct, sir.
- Q. And bearing in mind her date of death, sir, which would be around July of 1980, it would have been fixed in Klotz solution by the time you examined it for approximately 18 months?
 - A. Well I have ---
 - Q. January 1982.
- $\hbox{A.} \qquad \hbox{You might be right but I would}$ have to do estimations, $\hbox{sir.}$
- Q. Roughly around there. All right. The issue of embalming fluid doesn't come up here, sir, but I think you have indicated that age of the child had an impact on the digoxin results that you would get, is that correct?
- A. Are you referring to, which results, to heart tissue results?
 - Q. Heart tissue results.
- A. As I recall it I believe I mentioned that age is one of the factors that should be considered with respect to concentrations, for example, in the heart tissue, fresh autopsy heart tissue of children, that's right.
- Q. And I think the anomaly that you referred to was that if the same dose were given



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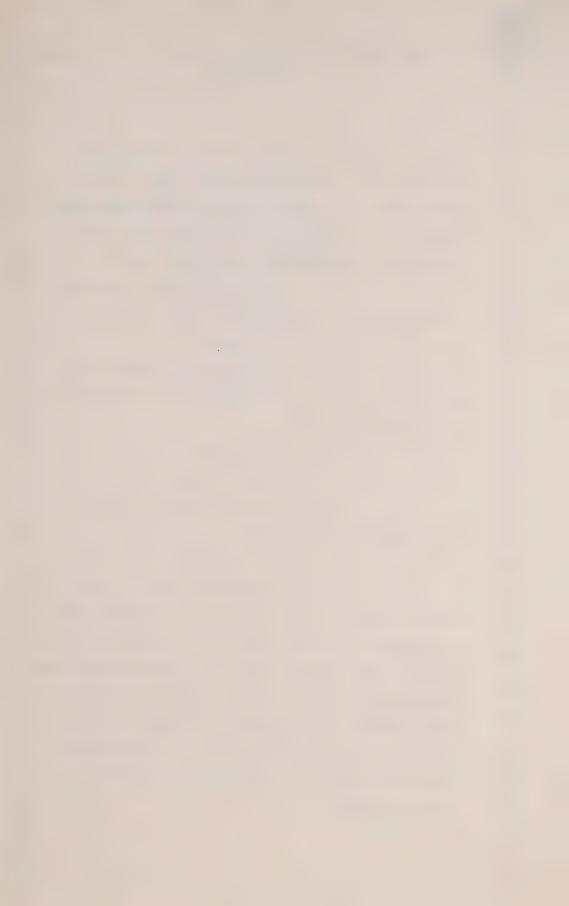
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we will say to a one month old child and to a one year old child, and fresh autopsy, heart autopsy samples were taken that you have observed that there seems to be a higher reading in the younger child of digoxin in heart tissue, am I right there?

- A. There may be, yes, there is a general trend to that effect, that is right.
 - Q. All right.
- A. Whether it be specifically the child, because I don't know until I would analyse it but there may be.
 - Q. I am sorry.
 - A. There may be.
 - Q. There may be, all right.

There appears to be a trend?

- A. That is right.
- Q. And finally, sir, I think without referring you specifically in Exhibit 213, it appeared to me that digoxin in the Klotz solution itself, if you recollect the chart that you had there it was left in Klotz solution I think for close to seven months; and the digoxin in general in samples that were in Klotz solution that over the passage of time the amount of digoxin and the reading of digoxin lowered?



Cimbura, cr.ex. (Shanahan)

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A. That's right, there was a decrease with time, that is right.

Q. And then you made a note

here, which is like a conclusion:

of the digoxin reading?

"From the data derived ..."

I am on the same page, sir, page 11:

"From the data derived from the T35,..."

and those are the tests that you did:

"...it is likely that the concentrations of digoxin in the heart and/or lung tissue before they were fixed in Kltoz solution were higher than the concentrations found."

A. . That is correct, sir.

Q. And that of course would

- just fit in with the last test, if you like, or sampling that you referred me to, and that was that you were working backwards 18 months fixed in Klotz solution and you assumed some lessening if you like
 - A. That is correct, sir.
 - Q. Leaving aside Dawson then,

THE COMMISSIONER: Before we leave

aside Dawson I would just like to make sure. What



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is the page in 213, the Klotz solution?

MR. LAMEK: 11.

MR. SHANAHAN: The page for Klotz alone

THE COMMISSIONER: That is the

diagram, isn't it?

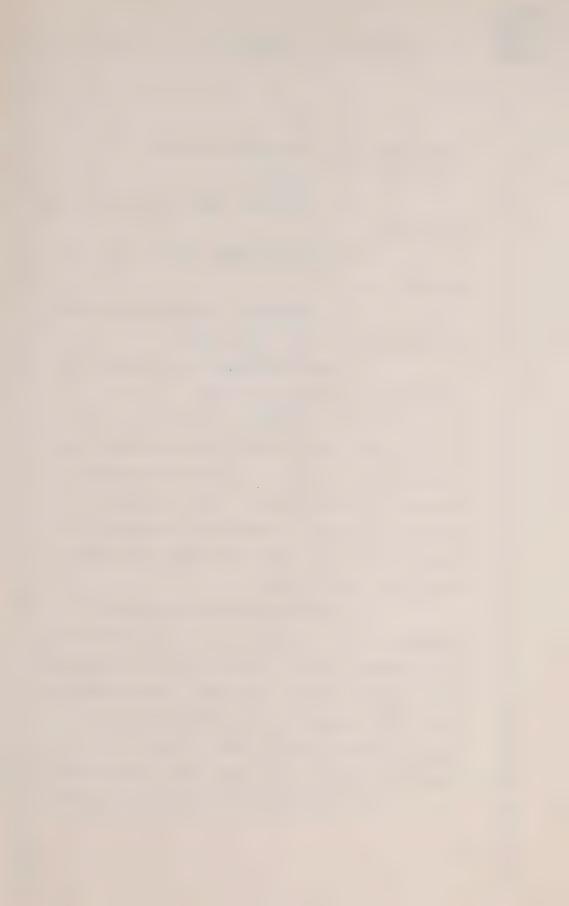
sir, is 11.

MR. SHANAHAN: "Stability of digoxin in Klotz solution", Mr. Commissioner.

THE COMMISSIONER: And you have, as far as period of storage 160 days.

MR. SHANAHAN: Well I think that page 13 as I read it, and I hope I have read these right then compares: Klotz, fixed heart and lung over a period of 6 to 9 months and I think that showed, and Mr. Cimbura will correct me if I am wrong, that seemed to show the fall-off in digoxin readings when it was fixed in Klotz.

THE COMMISSIONER: This may be fundamental, but you would make a test in which you get a reading of let's say 50 nanograms and then you do an HPLC test and it goes down to zero, that means all of the digoxinlike substances, all of the digoxin that you found is really digoxinlike, probably its product is digoxin, am I right so far? THE WITNESS: I assume that all the



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digoxin has degraded down, that's right. So that digoxin itself is below our detection levels.

THE COMMISSIONER: Your assumption in doing this is that it was all once digoxin, is that it, am I correct in that?

THE WITNESS: That is correct, sir.

MR. SHANAHAN: Q. I am afraid I

didn't hear you, Mr. Commissioner.

THE COMMISSIONER: The assumption is that it was all once digoxin and by refining it further you discover that it is now one of the offshoots of digoxin itself, is that right?

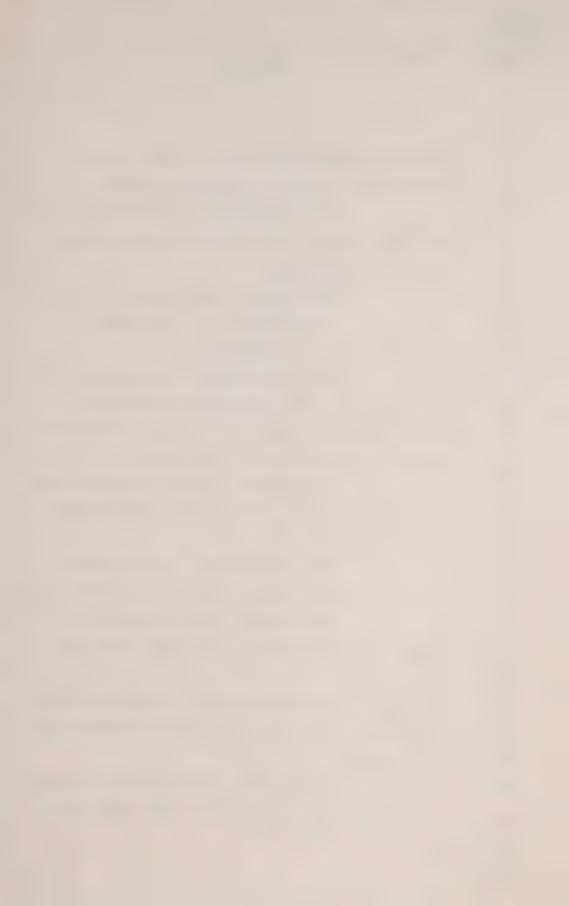
THE WITNESS: In some I am discovering it is just the offshoots of digoxin, that is right, but of course ---

THE COMMISSIONER: But you draw the conclusion I take it that it was once digoxin?

THE WITNESS: The assumption that I draw is that initially it was digoxin, that is right.

THE COMMISSIONER: Is there any way of comparing the, what is the chemical term for it, the offshoots?

THE WITNESS: The degradation products?
THE COMMISSIONER: Yes, what is it





called, I'm sorry, it is the end of the week, you have used it at least 28 times along here, these digoxin-like substances, the products of it, it doesn't matter what the term is. Have you any way of determining the amount of the digoxin that was there based upon the digoxinlike substances that you found, it is not the same amount I take it?

THE WITNESS: Oh, I would expect it to be higher in the beginning, that's right and the only estimation.

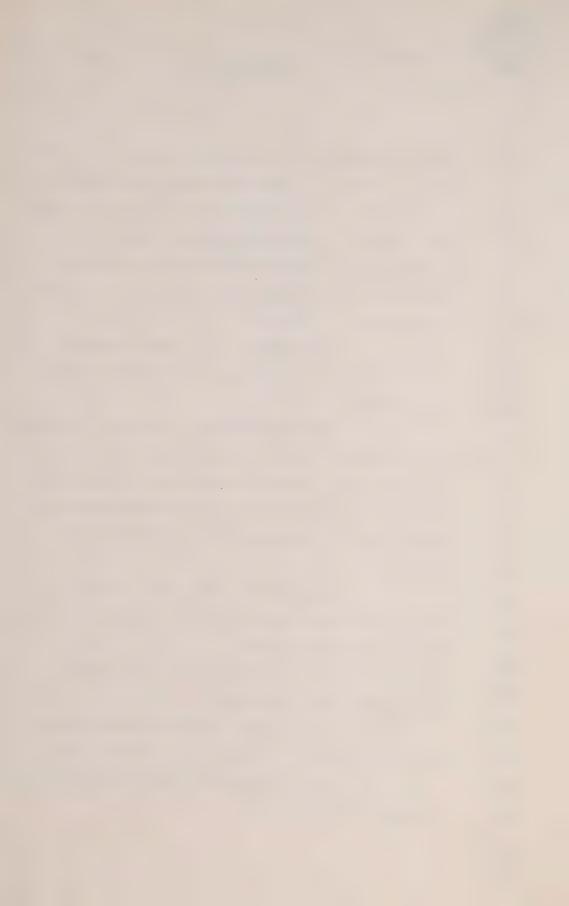
THE COMMISSIONER: If you get a reading in an RIA finding a figure of 50, and HPLC figure is zero, that is you have no digoxin there, but you know that there are 50 nanograms of digoxinlike substance, have you any way of calculating what the digoxin was at any time?

THE WITNESS: Well, yes. I have given that estimate with respect to tissues that were placed just by themselves.

THE COMMISSIONER: All you say is that it was greater than that?

THE WITNESS: In some tissues I have given an estimate of a minimum concentration, yes.

THE COMMISSIONER: Could you give me an example of that?



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THE WITNESS: Yes, sir.

THE COMMISSIONER: For instance you did in T35 the very one we are doing, Dawson?

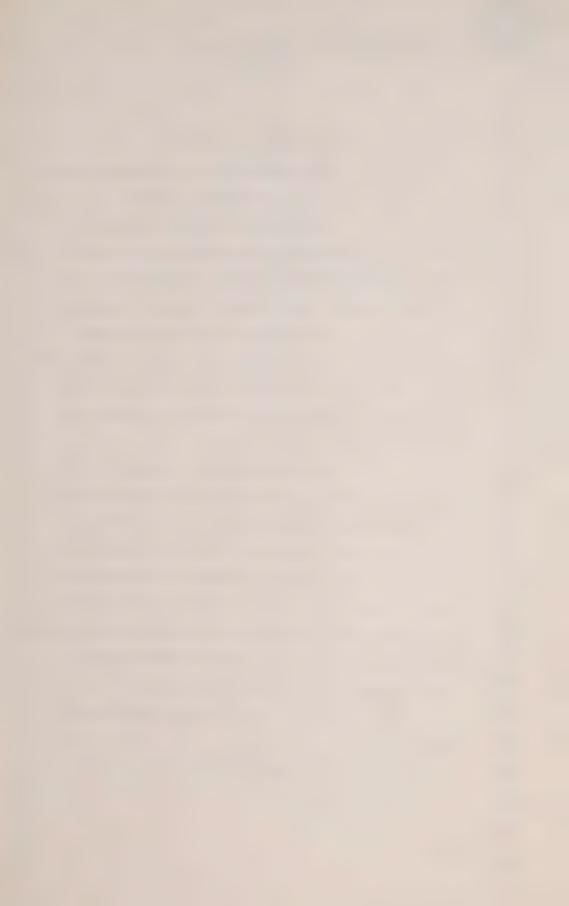
THE WITNESS: I couldn't do it here because there were two tissues placed into the container, and for that reason I couldn't get that estimate because I felt it would not be reasonable.

For example if you go to my page
7, which are tissues, which is the heart tissue alone
from a child Kristin Inwood; and on page 8 I draw,
I estimated a minimum concentration of digoxin in
the tissue before it was fixed.

THE COMMISSIONER: And that is the part in the heart, I don't want you to go into it too deeply but can you give me some idea how you calculated; for instance you have 323 of the mixture of digoxin and digoxinlike substances and this is the left ventricle; and you have got 230 nanograms of digoxin, poor digoxin at that point and you estimate then that the amount of digoxin in the heart was not less than 549, how would you do that?

A. Yes, sir, if I may explain

THE COMMISSIONER: Yes.





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THE COMMISSIONER: Yes.

THE WITNESS: I have multiplied, I have only used the concentrations obtained by the RIA for that purpose under the assumption that the digoxinlike substances were derived from digoxin.

THE COMMISSIONER: Yes.

THE WITNESS: So that I have multiplied the volume of the Klotz solution that I knew for example in the Baby Inwood. If you go to page 8 there is a volume 450 ml. This was the volume of the Klotz solution surrounding the tissue. I have multiplied that by the concentration in the Klotz tissue, in other words, by the 31 to give me a total amount of digoxin and/or digoxinlike substances in the Klotz medium surrounding the heart.

THE COMMISSIONER: All right.

THE WITNESS: I have divided this total figure into the weight of the heart of Kristin Inwood, the weight at the autopsy which would give me the nanograms per gram in the fresh heart tissue of Inwood. To that I have added the minimum amount that I have found in the regions of the heart, whatever was the lowest, and I came within an estimate as presented.

> THE COMMISSIONER: Yes, all right.



Thank you. You go on then, Mr. Shanahan.

right, thank you.

prior to its death for a day.

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tissue?

in general, just looked at them quickly and compared them to other exhumed tissue that you looked at and it seemed to me that in general Lombardo's readings were the highest readings that you got in exhumed

child that died in September of 1980 and it was 10

days old, had been in The Sick Children's Hospital

since the day of its birth and had been on the ward

MR. SHANAHAN: Can I take over, all

Q. Lombardo, Doctor, we know is a

Now, as I looked at Lombardo's readings

A. That is correct, sir.

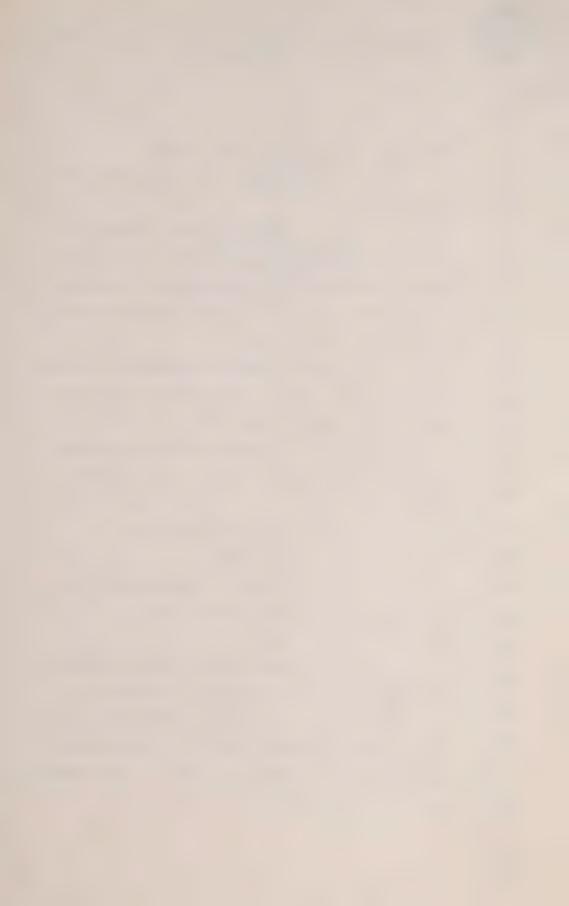
Q. All right.

A. At least in tissues that I am talking about are tissues such as heart.

O. Yes.

A. Lung, liver. Perhaps I should go to my report. Could you direct me to it.

Q. All right, I will direct you to it. We have it as Exhibit 95C, it is the report of March 25th, '82 and then it is page 2 of that report, sir.





GG.3

In general, sir, as I saw this as we looked at the development of testing for digoxin The Sick Children's Hospital were doing regular RIA assays on antemortem blood samples. It seemed to me then that you went into the area and they to some extent of postmortem blood and tissue with these reports that you have given us in 213 and the other evidence you gave us at your earlier testimony.

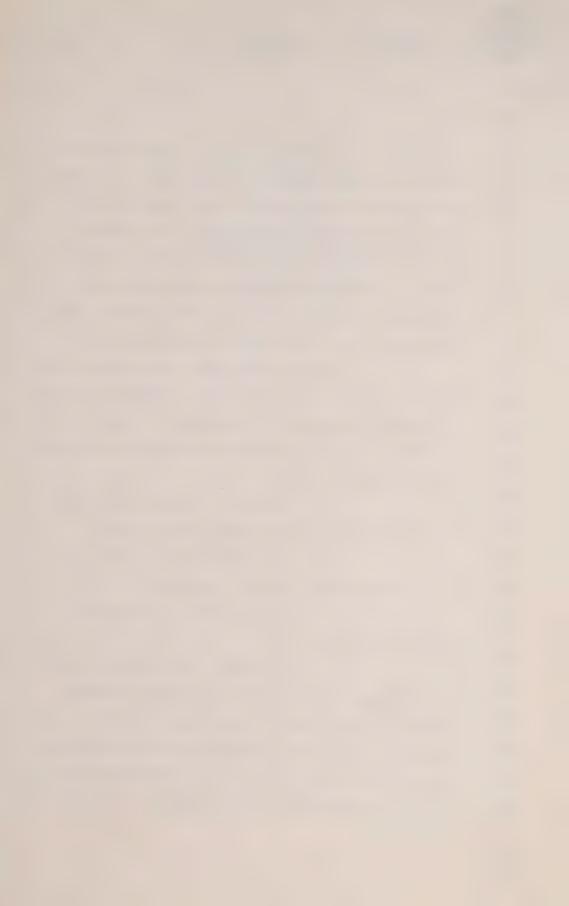
Then the third area that seemed to be the real problem area, or more of a problem area was that general area then that started to develop during the Nelles Inquiry of exhumed tissue and how you would approach exhumed tissue.

A. Approach - I think I know what you mean but approach from what point of view?

Q. Well, from testing. Just to even find digoxin let alone interpret it?

A. That's right, it posed some additional complications.

Q. All right. And then as I looked at that group of babies that had tissues exhumed,
Lombardo's really seemed to be unique from the perspective that, well, obviously it was never fixed in Klotz and it was also one of the children that I saw in the exhumed that was not embalmed. Is that correct?



GG.4

A. As far as I can recall, yes.

Q. That seemed to be your evidence too, I think it was yesterday it was given your evidence from the preliminary, your evidence was that the tissue of Lombardo had not been embalmed at all. All right?

A. Okay.

Q. Now, as I see it here the best of all samples would be of course the fresh from autopsy but it struck me, sir, and I appreciate there are problems with deterioration over 18 months to 2 years, but at least the Lombardo sample is not complicated in any way by Klotz solution, whatever complication that might be, or by embalming. It is really fresh tissue entombed for 18 months, 2 years, what-have-you.

A. With the result that it is not fresh any more after 18 months, yes.

Q. So, you have in Lombardo then not the problem if there is a problem with Klotz solution or the problem with embalming fluid, you have purely and simply that the massive problem, I agree, but the problem of degradation of this tissue in general?

A. Well, that is one of the problems.





GG.5

There are other problems.

Q. All right. And again here, sir, in terms of your overall experiments when you were dealing with blood and heart tissue here in Exhibit 213, it seemed to me that the general passage of time when you had digoxin in Klotz solution, for instance, over the passage of six to seven months there was a dramatic decrease in the amount of digoxin that was then in your sample?

A. There was a decrease, in some cases dramatic, yes.

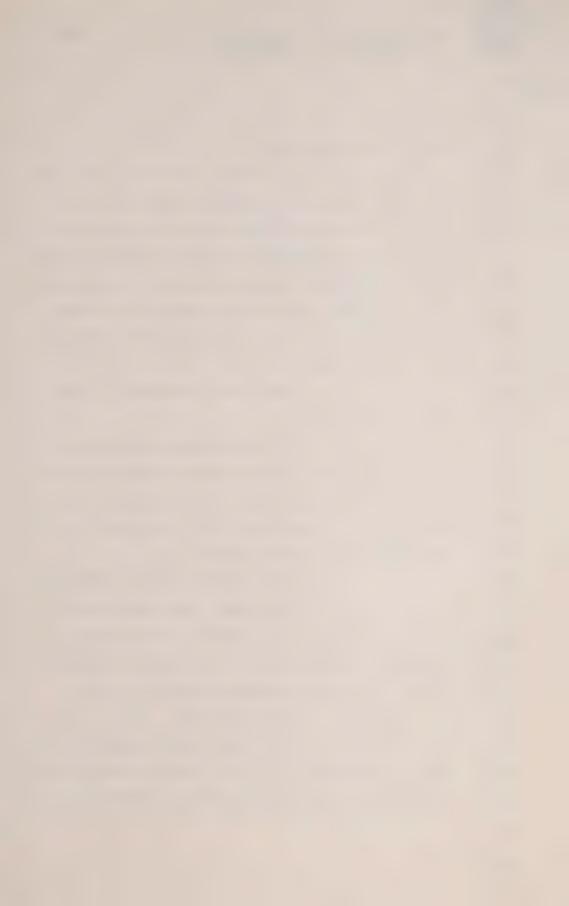
Q. In the embalming fluid as well in Exhibit 213 when you took digoxin embalming fluid and left it there for a period of time again there was a fall off, a large fall off in the amount of digoxin that was assayable there?

A. Under the conditions studied, yes.

Q. All right. And then finally tissue that was fresh and then put in Klotz and studied at a later point in time, again, you found a fall-off in the digoxin readings there as well?

A. That's correct.

Q. All right. Now, Lombardo of course is different and it is a jump, no question, but what you found, the readings that you found in



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Lombardo are clearly given what your recovery studies were and that you didn't compensate for the recovery factor, they are on the minimal, the conservative side, those readings that you have given us here. Am I right there?

A. That's what I would expect, that's right.

Q. All right. And I think you said as well as not compensating for the recovery factor that the recovery factor was higher in the high blood readings and, again, we are extrapolating from blood to exhumed tissue, but when you were talking about recovery factor and compensating, your recovery factor was even higher when you got into the higher readings?

I think I know what you want to say but I'm not sure if you're saying it correctly.

Q. All right, you say it right because I probably never will.

I think, if I am correct, are you saying that with the very high concentrations you may get lower recoveries?

- That's right. 0.
- You may, that's right, ves.
- All right. And you didn't compensate, so, what I'm saying is that the higher



GG.7

the reading got, and I'm looking here at T53 in Lombardo, there is 667 nanograms per gram of digoxin, that the higher the reading got it would even be more to the low side as you get into the higher regions?

- A. Well, I'm not really sure.
- Q. You're not sure?
- A. The extraction, the fact that the extraction was carried out, that would tend to make them minimal.
 - Q. All right.
- A. The other factors that are involved are factors such as, you know, dilution, small dilution errors when you have to dilute many times and they are unpredictable, they can go one way or the other.
- Q. I appreciate the dilution, yes, that can go one way or the other. But I did think that when you didn't compensate for recovery that that made your estimates minimal and conservative and then when I tied that in with another comment that the higher the dig. reading in blood mind you the lower the recovery rate and accordingly therefore that even more compensation would be needed, compensation upwards in the dig. reading?
 - A. Well, I'm not quite sure.



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A. I would have to look at that document again.

All right. In any event then as you test Lombardo you come to the conclusion here. sir, and that is on page 3 of the document I think you have found:

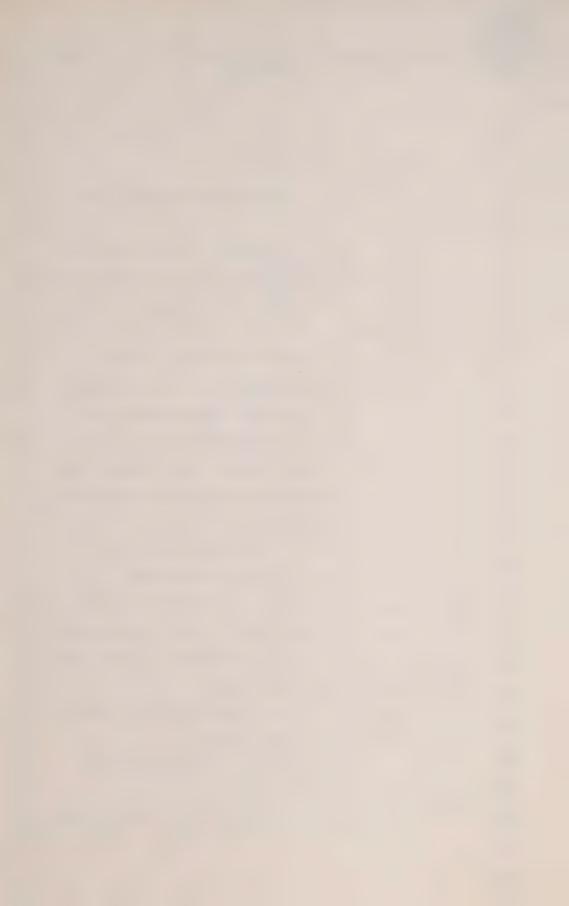
> "In view of the length of time the body had been buried it is difficult to assess the significance of the digoxin concentration found in the various tissues. Nevertheless, the possibility of digoxin poisoning must be considered in this case." There was no question, sir, in that

note that it may be difficult to assess the significance, there was no difficulty and there didn't appear to be any doubt in that note that the presence, the mere presence of digoxin in your mind was unequivocal, unquestionable?

- A. That the presence of digoxin ...
- That's right.
- Oh, yes, I expressed it as

digoxin, certainly.

Q. All right. Sir, I took it that





GG.9

you were firm in that conviction because	you had done
it not only by RIA, you had then done it	by RIA after
HPLC and you also with the Lombardo in a	combination
mixture I think of heart and lung tissue,	you also
used the mass spectrometry technique?	

A. That is correct, sir.

Q. All right. And all three confirmed for you the presence of digoxin and the RIA/HPLC actually gave you readings?

A. Well, the HPLC, you could almost say confirmed by digoxin.

Q. All right.

A. The GC mass spec. was an additional bonus, you could call it.

Q. There was no question about the presence of it. The significance was a problem. You conclude:

"Nevertheless, the possibility of digoxin poisoning must be considered in this case."

Moving ahead, sir, into some of the other children, and this would be Exhibit 95E on exhumed tissue, and I am not going to - you seem to get into a standard phraseology, sir, that differs really from what you concluded on Lombardo's. I will



GG.10

read one in full and that, sir, is the report of September 29th, Exhibit 95E, page 2, on the child Bilodeau. On page 3, the child here who had been embalmed, you say:

"3. The embalming process, the long burial period and the resultant decomposition may have influenced the digoxin concentrations to an extent which cannot be assessed with a reasonable degree of scientific certainty. For this reason, comparison of digoxin values in the exhumed autopsy material with those of 'fresh' autopsy tissues may not be valid."

And then you conclude:

"In view of this and other factors, the results obrained in this case are considered inconclusive with respect to digoxin toxicity."

And, sir, as you go on to others,

Gionas, Barbara Gionas follows, you conclude in

paragraph 3 the same wording again: " ... inconclusive

with respect to digoxin toxicity." for the same factor.

Inwood follows

and it has the same, and many others do.



Was Lombardo, just because it was done earlier, different wording, or does it indicate, as I read it, that with Lombardo, because of the very high readings you are prepared to go even further than you did in those other children that I mentioned, and there were more I could have taken you through there, and be able to conclude that digoxin poisoning had to be considered.



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	A.	Well,	first o	f all,	to ar	nswer
your question	, the di	fferent	way of	expre	ssing	the
notes is main	ly becau	se of d	differen	ce in	time	
between the to	wo repor	ts.				

 $\Omega.$ There is no particular magic to the wording?

A. Pardon me?

 Ω . There is no particular magic to the wording, as you got later you just seemed to fall into that pattern.

A. At that time we had a whole group of children that had been exhumed. Baby Lombardo was more or less isolated at the earlier time.

Ω. That's what I thought, yes.

A. And it was later on in time and by that time I reached a definite conclusion that the results in the exhumed tissue are by themselves inconclusive; inconclusive meaning of course, as I would appreciate and I'm sure you know that, it may or may not be, I cannot rule out the possibility.

Ω. I understand. It just struck me as more doubt came into the air around April, September, December of '82 you weren't prepared to be as definitive.



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others	was	that,	as yo	u sa	aid,	chil	d Lo	mbaro	do v	vas
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- Ω. Right. Well then, this is the final series or set of questions. Lombardo was prescribed digoxin and wasn't embalmed, as we see here. It seems to me, sir, that we are never going to be able to set up a protocol, if you like, for ever finding out the meaning of readings in exhumed tissue from a child like Lombardo. It may be obvious because you would have to get a child and give it digoxin by either therapeutic or overdose, not embalm it.
- A. Well, you could have a child who died accidentally with a digoxin overdose, that's right.
- Q. All right. But all the other circumstances really are almost in a laboratory settingimpossible to reproduce.
 - A. I agree, yes.
- 0. The fact of no embalming, wait for a couple of years.
 - A. I agree.
 - 0. Is that right?



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course of	exhuming	the	child	for	the	pui	rposes	of	
the resear	rch.								

- Q. That's right.
- A. I don't think it is possible.
- Ω . No.

THE COMMISSIONER: Would the

exhuming do it?

happen.

THE WITNESS: I beg your pardon?

THE COMMISSIONER: What would the exhuming do itself?

THE WITNESS: To study what may

THE COMMISSIONER: No, no, I know you would have to do that.

MR. SHANAHAN: I think he meant storage conditions. You are not at room temperature, you are not in a fridge, you are sort of in that whole, whatever entombing does to tissue.

THE COMMISSIONER: All right. But tell me this. If a child never did have digoxin, could there be digoxin found in its tissues after any amount of time?

THE WITNESS: I don't know how, sir.

THE COMMISSIONER: Where would it



come from?

THE WITNESS: I don't know how, sir.

I don't believe so, no.

I mean, it might have been a very small amount of digoxin that you had, but could it get it any way in any natural process that you know of? You may not be able to answer this question.

THE WITNESS: As far as I know, no endogenous digoxin itself is produced in the body.

THE COMMISSIONER: No, but the process of decay itself, would it not, as far as you know?

THE WITNESS: As far as I know there would be nothing published on that, there would be no reports on that.

THE COMMISSIONER: I see, all right.

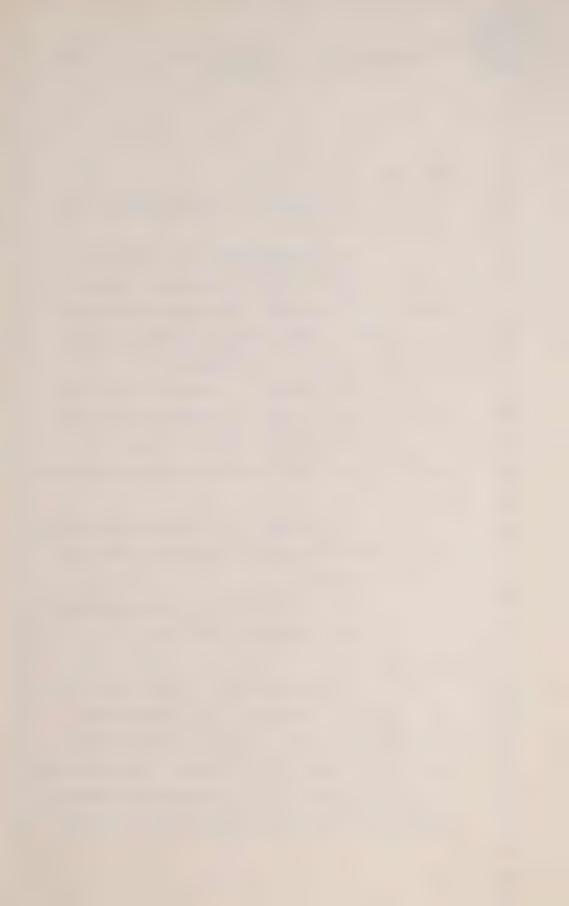
MR. SHANAHAN: All right,

Mr. Commissioner?

THE COMMISSIONER: Yes.

MR. SHANAHAN: Q. And then one final thing then, sir. In terms of us never being able to really reproduce the Lombardo situation again, as you carried what the Sick Children's had done in normal - in life blood testing and then you carried

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it into and refined the techniques with respect to tissue and then after death post mortem and then to go from there into the area of Lombardo which was tissue not preserved, not embalmed, just simply if you like set aside for a year or two and the readings that you got, in all other areas, by the Lombardo, the exhumed tissue area, with the passage of time, be it embalming fluid, Klotz fluid or what, fresh and then fresh gone into fixed in Klotz, in all other samples digoxin did what I as a layman would anticipate and, that is, that with the passage of time it lessened in tissue and in blood.



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 Ω_{\bullet} All right. So we would be asking you or someone else to make the leap then and to say and to infer it would only be a leap or

Α.

preserved in chemical preservatives.

and to say and to infer it would only be a leap or a guess as to whether in tissues such as Lombardo's that hadn't been embalmed and had not been fixed as to whether in fact digoxin would fall from the point of having the dose to a point in time two years later when it would be looked at by your RIA and HPLC and

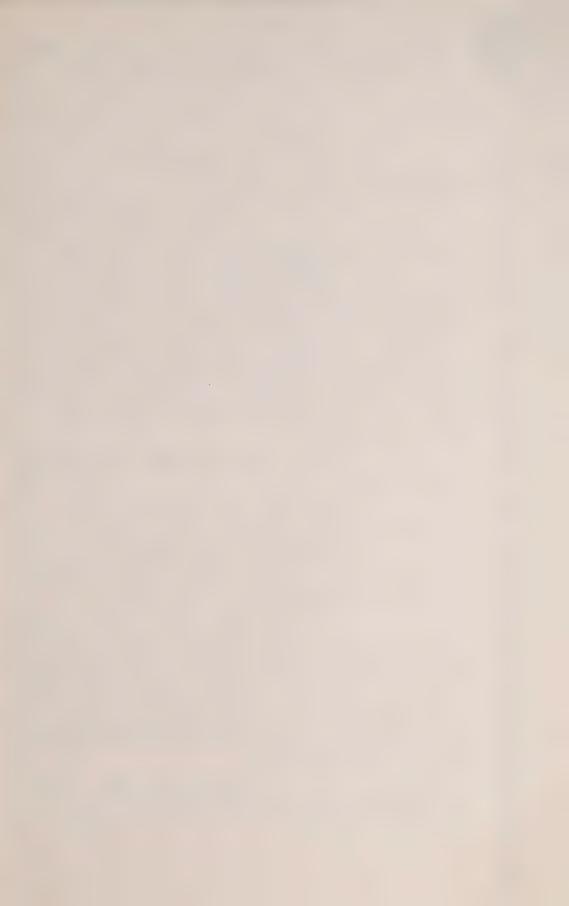
A. That is right, it would be a guess I feel.

But there is another factor, of course, to be of concern and that is with a burial, long burial, there may be a drying of tissue to some degree which would tend to go the other way.

In other words if there was a drying, it would tend to artificially increase the levels as compared to what they were at the beginning.

 Ω . As fluid dried out of the body and the body tissues, the remaining concentration of digoxin may be inflated?

A. That is right. When expressed per nanogram per weight, that is right.



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in	all	oth	er	areas	digo	oxir	ove	c ti	me l	essens	in	the
rea	ading	js i	ln i	tissue	and	in	blood	?				

A. In preserved tissues.

0. And certainly, sir, therapeutic doses in life did not produce for you in fresh or fixed autopsy samples, did not produce the readings that you found in Lombardo?

A. Would you repeat that again?

Therapeutic doses in some 0. of the experiments that you recorded in Exhibit 213, therapeutic doses in life of a child did not produce readings in tissue that you found in the Lombardo child after exhumation?

Well, one couldn't

There was a very general statement that would have to be broken down, you know, into more detail. I know what you are attempting to say but before I could comment we would have to break down piece by piece.

And of course again as you Q. said before you would have to make the leap between tissue that was fresh and tissue that was exhumed?

> That is right. Α.



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MR. SHANAHAN: Thank you, sir.

THE COMMISSIONER: Mr. Shinehoft,

please.

CROSS-EXAMINATION BY MR. SHINEHOFT:

 Ω_{\bullet} Mr. Cimbura, my name is Jack Shinehoft and I represent the parents of Kevin Pacsai.

I understand, doctor, that you have indicated to us that your profession is that of a forensic toxicologist; is that correct?

A. That is my specialty,

that is right, sir.

that is correct.

report, sir?

Q. And as part of that job do you analyze blood and tissue samples?

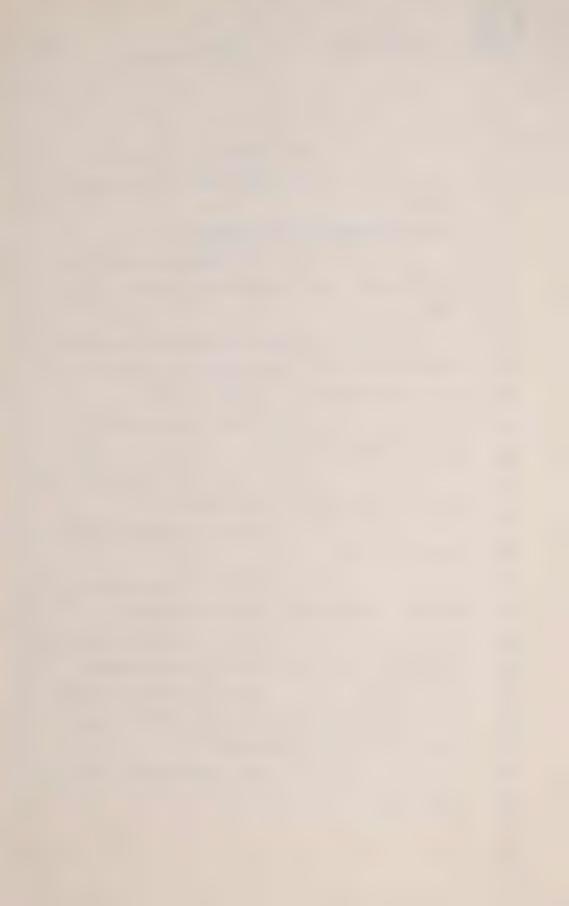
A. Blood and tissue samples,

Q. Do you do that for the purposes of determining the cause of death?

A. For the purposes of assisting to determine the cause of death, that is right.

Q. And you indicated that you did these blood and tissue samples as far as the child Kevin Pacsai is concerned?

A. You are referring to my



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		Q.		Yes,	sir.	You	did	those
analyses	as	indicated	in	your	report	?		

A. They were done in my laboratory, that is right, sir.

- Q. Under your supervision?
- A. That is right.
- Q. And did you come to a conclusion as to the cause of death as far as Baby Kevin Pacsai is concerned?
- A. Well, cause of death is not my function.
- Q. Well, correct me if I am wrong but didn't you just tell me, doctor, that -
 THE COMMISSIONER: He specifically said to assist in determining the cause of death.

 MR. SHINEHOFT: Okay.

Q. And did you come to a conclusion as to the cause of death as far as this baby is concerned?

THE COMMISSIONER: That is what he is trying to do here. He is trying to help us.

MR. SHINEHOFT: Yes.

Q. But you have done some testing and you have got some results and presumably you interpret those results, do you not?



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A. With some respect, that is

right, sir.

my report?

Q. And how did you interpret the results that you found?

A. Do you wish me to go into

Q. Yes. Basically did you come to a conclusion as a result of the test data or the results that you ascertained?

A. Yes, I recall the findings but I would just like to have a look at my report to make sure.

Q. Oh, sure.

THE COMMISSIONER: On page 5.

THE WITNESS: Yes, that is right.

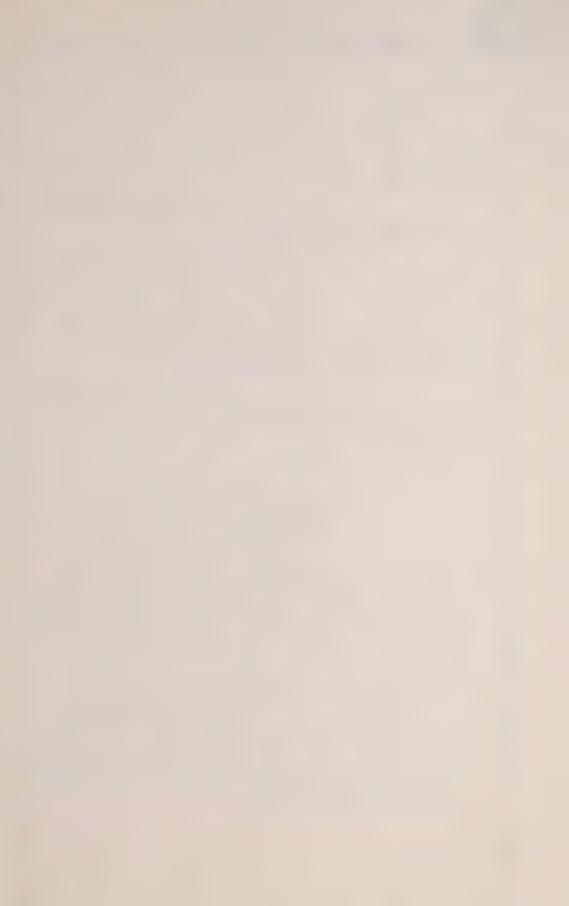
There is a sample -- there is a

specimen of serum which I understand was obtained post mortem from the Child Pacsai and that specimen was found to contain 26 nanograms per millilitre of digoxin.

MR. SHINEHOFT: Q. Yes.

A. This value is within the fatal range of values for blood or serum. And for that reason in my opinion it could account for death.

It could account for death.



Q. Okay. Now you came to that conclusion I believe sometime in 1981; is that correct?

A. That is correct, yes.

Q. And has that opinion changed from 1981 to today as far as that is concerned?

A. No, sir.

Q. You feel qualified to comment on the value that you obtained, this reading of 26, on how that reading came about in the context that it could have come about by a mistake or accidental overdose or is it possible that it came about by deliberate overdose?

Now, first do you feel you are qualified to give an answer to that question?

A. I cannot, no. From my findings it doesn't tell me whether it was given or taken accidentally or deliberately.

Q. All right.

A. Lt doesn't permit me to

Q. But you do and you did come to the conclusion that the amount of 26 nanograms is a toxic amount which could account for this child's death?

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A. It could account for this child's death, that is right.

 Ω . And --

A. In combination with another finding which we haven't gone into but I have taken both into consideration, that is right.

Q. You took the tissue sample into consideration as well, doctor?

 $\hbox{A.} \qquad \hbox{There was one tissue sample}$ in the -- let me find it.

Q. Tissue sample, I believe on

 $\label{eq:A.} \text{Not really that one.} \quad \text{There}$ is another tissue sample --

MS. CRONK: Page 5, September 29.

A. On page 5 of my report of

MR. SHINEHOFT: Q. Yes. That is your tissue sample?

A. Yes. This is a little bit different tissue sample since it was reported to me to be -- to have been kept frozen at the Hospital until I received it, which would make it equivalent to fresh autopsy sample.

Q. Okay.



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			Α.	And	tha	t tiss	ue v	which
was	a lung	tissue,	, the	tissue	e was	found	to	contain
122	nanogra	ms per	gram	of dig	goxin			

Q. Okay.

A. This value is also elevated as compared to controls. By itself this value would not be conclusive in my view to digoxin toxicity but in combination with the previous finding it permitted me to give an opinion that I believe the findings could account for cause of death as a possibility.

Q. All right. Did you in your analysis of both blood and tissue samples come to any other possible conclusions or any other possible determination of the cause of death or possible cause of death of Kevin Pacsai other than what you have stated to us?

A. As I recall it these were the more essential findings.

Q. I am not talking about findings. I'm talking about -- you said you did certain tests and you got certain values and you came to the conclusion based on those values that a possible cause of death may have been digoxin toxicity.

Is that correct, Mr. Cimbura?



Cimbura cr.ex. (Shinehoft)

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нн9	2,	A. Yes, possible cause of
	3	death.
	4	Q. Was there any other
	5	possible cause of death that you could determine
	6	from your analysis of the tissue and blood samples
	1	that were submitted to you?
	7	A. That is not my function.
	8	That would be somebody else's function.
	9	Q. Well, I'm just asking you.
	10	A. No.
	11	MR. SHINEHOFT: Thank you very
	12	much. Those are all the questions I have.
	13	THE COMMISSIONER: Thank you very
	14	much, Mr. Shinehoft.
		MR. HUNT: I have no questions.
	15	THE COMMISSIONER: Mr. Lamek?
	16	MR. LAMEK: Mr. Commissioner, I have
	17	and I confess it is not really my question
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RE-DIRECT EXAMINATION BY MR. LAMEK:

Mr. Cimbura, could you turn with me, please, to page 11 of Exhibit 213, the digoxin stability graph in Klotz solution.

> Α. Yes.

The reference to the blip that occurs in each of those curves at about, oh, between 30 and 40 days; increases over the space of the next 10 days or so and then goes into a downward trend again.

> Yes, sir. A.

Were these assays done, and 0. the times of them are indicated, solely by RIA or was an HPLC technique used prior to RIA?

These were done RIA only.

0. RIA only? As I recall it vesterday I think you said - I think it was to Mr. Roland - that a blip could be accounted for by the appearance of some breakdown product of digoxin?

That was - I believe I stated A. I have no proof of that. it was a hypotesis.

> 0. All right.

But there is a possibility that at this particular stage of time there is some re-equilibrium of the degradation products to those



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which are a little bit more reactive to the RIA at the time.

Q. In fact had there been an HPLC separation done prior to the RIA we might have known whether there were any degradation products involved in this, might we not?

A. Well, if we had HPLC then we would have known the digoxin concentrations alone.

MR. LAMEK: I have no further questions of Mr. Cimbura.

Thank you very much.

THE COMMISSIONER: All right.

MR. LAMEK: I do have one thing if

I may, please.

I think I misled my friend Mr. Olah this morning with respect to the Inwood sample which yielded 491 nanograms. You will remember, Mr. Cimbura and Mr. Commissioner, I said it was my recollection that it was a sample that had come from the Haemotology Department. That of course was not so.

The Haemotology Department sample was the antemortem sample which upon analysis yielded a nil result of digoxin. I don't know the source of the 491 sample I am afraid.



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THE COMMISSIONER: Was that the one, though, that was heated?

MR. LAMEK: That is apparently the one that was heated. That is Mr. Cimbura's recollection of that.

THE COMMISSIONER: But it was the haemotology one that was heated?

MR. LAMEK: No, the haemotology one apparently was not ---

THE COMMISSIONER: I see.

MR. LAMEK: It was the one which eventually yielded 491 which is I gather a postmortem sample.

THE COMMISSIONER: All right.

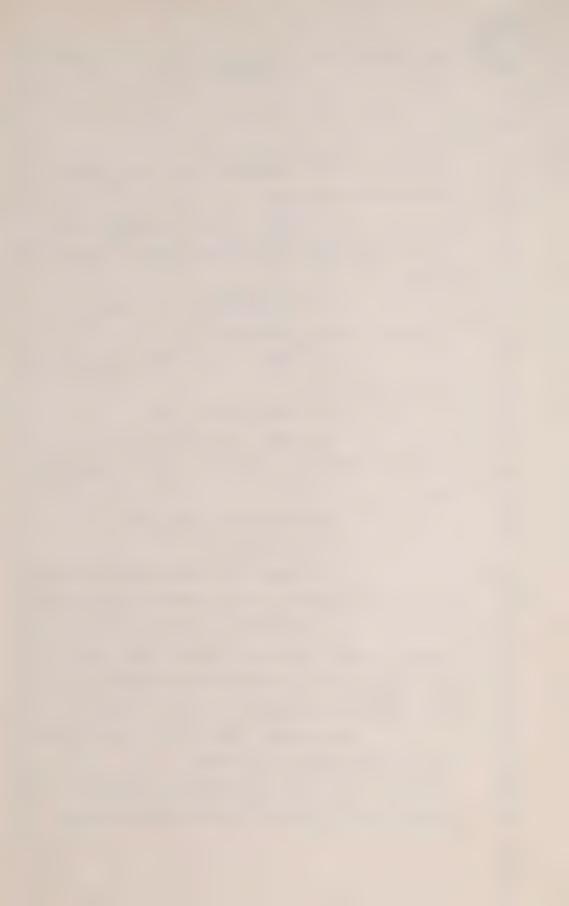
Yes, Mr. Tobias?

MR. TOBIAS: Mr. Commissioner, it might be helpful for counsel if we intended to prepare over the weekend if we could get some indication from Commission counsel as to the witnesses that will be called next week and the days of the week in which it is now anticipated they will be called.

MR. LAMEK: Yes, indeed. I don't know how much preparation will be done.

On Monday I propose to call Dr.

Speilberg who is a clinical pharmacologist at the



our spy.

Hospital for Sick Children. He may or may not take a week.

If Dr. Speilberg is completed before the end of the week then the expectation is Dr. Phillips, the pathologist from the Hospital will be called next, and the following week I propose to call Dr. Bain although at the beginning of the week since I understand I will be elsewhere learning the mystery of things, and it may be that Dr. Izukawa ---

THE COMMISSIONER: Saying hello to my colleagues, I understand, my former colleagues.

MR. LAMEK: No, I am with your former colleagues at the end of next week, sir.

THE COMMISSIONER: Oh, I see.

MR. LAMEK: Then the week after I expect to be with the colleagues of Dr. Speilberg.

THE COMMISSIONER: Oh, yes, you are

MR. LAMEK: I am a spy, that is right.

So then next week the batting order is Dr. Speilberg, and if there is time, Dr. Phillips, and for the week after either Dr. Phillips and perhaps Dr. Izukawa at the beginning of the week followed by Dr. Bain.





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MR. HUNT: Mr. Commissioner, could

I just indicate that the inventory of specimens that
remain at the Centre for Forensic Sciences has
been completed and I have provided a copy of it to
Mr. Lamek, I don't know whether it needs to be
filed as an exhibit or not.

I take it that there has still been no formal request made of you for the release of any specimens until that occurs and the matter is discussed I take it it is satisfactory for the specimens that are still at the Centre remain there.

THE COMMISSIONER: Yes, yes, that is my understanding too, but at some point perhaps Dr. Soldin and Mr. Cimbura might discuss it, discuss the problem but nothing need to be done until there is some kind of formal application and a ruling.

Until 10 o'clock Monday morning then, that is for everybody except you, Mr. Cimbura.

THE WITNESS: Thank you.

---Witness withdraws.

---Whereupon the hearing adjourned at 4:45 p.m. until Monday, October 24th, 1983 at 10:00 a.m.



